

pons 816, which is the part of the brainstem that joins the hemispheres of the cerebellum and connects the cerebrum with the cerebellum, located just above the medulla oblongata;

5 a spinal cord 818, which is a thick bundle of nerve fibers that runs from the base of the brain to the hip area, through the spine (vertebrae);

a temporal lobe of the cerebrum 820, which is the region at the lower side of each cerebral hemisphere, located at the sides of the head and containing centers of hearing and memory.

10 The brain 215 may include a pathological feature 213, termed herein an organ target 213. A region-of-interest (ROI) 200 may be defined so as to encompass the brain 215 and the pathological feature 213.

As seen in Figure 57B, the region-of-interest 200 of Figure 57A is modeled as a model 250 of a volume U, and the organ target 213 is modeled as a modeled organ targets HS. Additionally, there are certain physical viewing constraints, associated  
15 with the region-of-interest 200, which are modeled as anatomical constraints AC. In the present case, the skull 830 creates viewing constraints, and generally, imaging the brain is performed extracorporeally.

Referring further to the drawings, Figure 58 pictorially illustrates a method  
340 for zooming in on a suspected pathological feature, as a process of two or more  
20 iterations, in accordance with embodiments of the present invention, as follows:

As seen in Figure 58, the method 340 may be described, pictorially, as follows:

In I: The region-of-interest 200, associated with the organ 215, such as the brain 215, is defined for the body section 230.

25 In II: The model 250 of the volume U is provided for the region-of-interest 200, possibly with one or several of the modeled organ targets HS, and within the anatomical constraints AC, for obtaining the optimal set of views for the region-of-interest 200. The optimal set of views is then applied to the region-of-interest 200, encompassing the brain 215 of the body section 230.

30 In III: When the suspected organ target 213 is identified, in vivo, in the brain 215, by radioactive-emission measurements at the optimal set of views, a second, inner region-of-interest 200' is defined, encircling the suspected pathological feature. For example, if a suspected pathology 213 is identified in the occipital lobe 810 of the

cerebrum, that is, the region at the back of each cerebral hemisphere at the back of the head, the second region-of-interest 200' is defined so as to encircle the occipital lobe 810 of the cerebrum.

In IV: A model 250' of a volume U' is provided for the second, inner region-of-interest 200', preferably, with at least one modeled organ target HS, simulating the suspected organ target 213, for obtaining an optimal pathology set of views for the region-of-interest 200'. The second, pathology set of views is then applied to the second, inner region-of-interest 200' of the body section 230. In the present example, the second, pathology set of views is then applied to the occipital lobe 810 of the cerebrum, in vivo.

Referring further to the drawings, Figures 59A – 60J schematically illustrate a camera system 850 for the brain, in accordance with a preferred embodiment of the present invention.

Figures 59A – 59C schematically illustrate the radioactive-emission camera for the brain, in accordance with embodiments of the present invention;

Preferably, radioactive-emission camera 850 for the brain is shaped as a helmet 860, adapted for wearing on a head 862. The helmet 860 is preferably mounted on a gantry 870, which may be adjustable in the directions of arrows 872, 874 and 876, for adapting to individual heights and comfort requirements.

Alternatively, no gantry is used, and the helmet 860 may be worn directly on the head 862, for example, like a motorcycle helmet.

A chair 880 may be provided for the comfort of the patient.

Preferably, the radioactive-emission camera 850 for the brain is operable with a control unit 890, which may be a desktop computer, a laptop, or the like. The control unit 890 is preferably used both for controlling the motions of the detecting units 12, blocks 90 and assemblies 92 of the radioactive-emission camera 850 for the brain and for analyzing the data.

It will be appreciated that the radioactive-emission camera 850 for the brain may be supplied merely as the camera helmet 860 and a data storage device, such as a CD 892, a disk 892, or the like, containing the appropriate software, for operation with an existing computer, at the site.

It will be appreciated that the present camera system for the brain may also be used as a PET system, for coincident counting.

It will be appreciated that the radioactive-emission camera 850 for the brain may be operable with a structural imager, as taught by commonly owned PCT publication WO2004/042546, whose disclosure is incorporated herein by reference. The structural imager may be a handheld ultrasound imager, possibly with a position-tracking device, a 3-D imager such as an ultrasound imager, a CT imager, or an MRI imager, as known. The data provided by the structural imager may be used for any one or a combination of the following:

- i. obtaining accurate dimensional data for modeling the brain 215, as taught with reference to Figures 57A - 58 and 11 - 12;
- ii. providing attenuation correction for the radioactive-emissions, based on the structural data, as taught by commonly owned PCT publication WO2004/042546; and
- iii. co-registering the functional and structural images, as taught, for example, by commonly owned PCT publication WO2004/042546.

Referring further to the drawings Figures 60A – 60K schematically illustrate inner structures of the camera 850 in accordance with several embodiments of the present invention.

Figure 60A schematically illustrates the assembly 92, comprising, for example four of the blocks 90, adapted for oscillatory motion about the r-axis, as illustrated by the arrows 50, and adapted for rotational motion about the x-axis, as illustrated by the arrow 62, as taught, for example, with reference to Figures 22A – 22H. It will be appreciated that detecting units 12 may be used in place of blocks 90.

Figure 60B schematically illustrates a possible cross sectional view of the camera 850 (Figure 59C), showing an arrangement of the assemblies 92, laterally around the head 862.

Figure 60C schematically illustrates a top view of the camera 850, showing an arrangement of the assemblies 92, laterally around the head 862. It will be appreciated that the number of the blocks 90 may vary around the head 862.

Figures 60D and 60E schematically illustrate other possible cross sectional views of the camera 850, showing arrangements of the assemblies 92, vertically around the head 862.

Figure 60F schematically illustrates the camera 850 formed as the helmet 860, with the assemblies 92, arranged as illustrated by the cross sectional view of Figure

60E. It will be appreciated that other arrangements are similarly possible. Preferably, the camera helmet 860 includes an overall structure 864. Preferably, the motions of the blocks 90 and of the assemblies 92 are contained within the overall structure 864.

5 Preferably, the proximal side of the overall structure 864 with respect to the head 862 (Figure 59C) is transparent to nuclear radiation. Alternatively, the proximal side with respect to the head 862 is open.

Figure 60G schematically illustrates another arrangement of the blocks 90 around the head 862, wherein the blocks 90 are not arranged in assemblies 92; rather  
10 each block 90 moves as an individual body. It will be appreciated that the detecting units 12 may be used in place of the blocks 90.

Figures 60H – 60K schematically illustrate possible rotational motions of the blocks 90, each of the blocks 90 moving as an individual body for obtaining views of different orientations. As seen in Figure 60H, the block 90 rotates around x as seen  
15 by an arrow 852 and at each position around x, oscillates about x, as seen by an arrow 851. The resultant traces are seen in Figure 60I as a star of line traces 854.

Alternatively, as seen in Figure 60J, the block 90 rotates around y as seen by an arrow 853 and at each position around y, oscillates about x, as seen by the arrow 851. The resultant traces are seen in Figure 60K, as line traces 855.

20 The assembly 92 and the block 90, in accordance with a preferred embodiment of the present invention are described in Figures 49A and 49B, hereinabove.

Thus the assembly 92 includes a row of at least two blocks 90, each adapted for oscillatory motion about r. The blocks 90 are arranged within the internal structure 21.

25 A motor 88 and a shaft 85 form the motion provider 76, while a secondary motor 86 and a secondary shaft 84 form the secondary motion provider 78, for the oscillatory motion about r. A plurality of motion transfer systems 74, for example gear systems, equal in number to the number of blocks 90, transfer the motion of the secondary motion provider 78 to the blocks 90. The motion transfer systems 74, of  
30 gears, make it possible to provide the row of blocks 90 with any one of parallel oscillatory motion, antipodal oscillatory motion, or independent motion, depending on the gear systems associated with each block 90. It will be appreciated that other motion transfer systems, as known, may be used.



It will be appreciated that detecting units 12 may be used in place of blocks 90.

In accordance with the present example, adjacent blocks 90A and 90B may move in an antipodal manner and adjacent blocks 90C and 90D may move in an antipodal manner, while adjacent blocks 90B and 90C may move in parallel. It will be appreciated that many other arrangements are similarly possible. For example, all the pairing combinations of the blocks 90 may move in an antipodal manner, all the blocks 90 may move in parallel, or the blocks 90 may move independently. It will be appreciated that an odd number of blocks 90 may be used in the assembly 92.

It will be appreciated that imaging, in accordance with embodiments of the present invention relates to the imaging of the whole brain, or to a portion of the brain, or to blood vessels near the brain, for example, the coronary artery.

Preferably, the radiopharmaceuticals associated with the camera of the present invention may be Tc99m-d, 1-hexamethyl propylene amine oxime (1-HMPAO) commercially known as Ceretec by GE-Amersham, or Tc-99m-ECD, commercially known as Neurolite, and made by Bristol Myers Squibb.

The present invention applies to the two types of brain tumors: primary brain tumors, which originate in the brain and metastatic (secondary) brain tumors that originate from cancer cells that have migrated from other parts of the body.

Additionally, the primary brain tumors may be gliomas, which begin in glial cells, and of which there are several types, as follows:

Astrocytoma, a tumor which arises from star-shaped glial cells called astrocytes, and which in adults, most often arises in the cerebrum, whereas in children, it occurs in the brain stem, the cerebrum, and the cerebellum.

Brain stem glioma, a tumor that occurs in the lowest part of the brain, and is diagnosed in young children as well as in middle-aged adults.

Ependymoma, a tumor, most common in middle-aged adults, which arises from cells that line the ventricles or the central canal of the spinal cord and which occurs in children and young adults.

Oligodendroglioma, a rare tumor, which arises from cells that make the fatty substance that covers and protects nerves and usually occurs in the cerebrum, grows slowly and generally does not spread into surrounding brain tissue.

Additionally or alternatively, the present invention applies to other types of brain tumors, which do not begin in glial cells. The most common of these are:

Medulloblastoma, also called a primitive neuroectodermal tumor, a tumor which usually arises in the cerebellum and is the most common brain tumor in children.

Meningioma, which arises in the meninges and usually grows slowly.

5 Schwannoma, also called an acoustic neuroma, and occurring most often in adults, it is a tumor that arises from a Schwann cell, of the cells that line the nerve that controls balance and hearing, in the inner ear.

Craniopharyngioma, a tumor which grows at the base of the brain, near the pituitary gland, and most often occurs in children.

10 Germ cell tumor of the brain, a tumor which arises from a germ cell, generally, in people younger than 30, the most common type of which is a germinoma.

Pineal region tumor, a rare brain tumor, which arises in or near the pineal gland, located between the cerebrum and the cerebellum.

15 Additionally or alternatively, the present invention applies to tumors associated with certain inherited diseases, for example, Multiple endocrine neoplasia type 1 (pituitary adenoma), Neurofibromatosis type 2 (brain and spinal cord tumors), Retinoblastoma (malignant retinal glioma), Tuberous sclerosis (primary brain tumors), and Von Hippel-Lindau disease (retinal tumor, CNS tumors), and genetic mutations and deletions of tumor suppressor genes (i.e., genes that suppress the  
20 development of malignant cells), which increase the risk for some types of brain cancer.

Additionally or alternatively, the present invention applies to tumors associated with exposure to vinyl chloride.

25 Additionally or alternatively, the present invention applies to secondary brain cancer, for example, originating from the lungs, the breasts, or other parts of the body.

It will be appreciated that the present invention further applies to other types brain tumors, which may be malignant or benign, blood clots in the brain, and other brain pathologies. It will be appreciated that many other cameras and camera systems may be considered and the examples here are provided merely to illustrate the many  
30 types of combinations that may be examined, in choosing and scoring a camera design, both in terms of information and in terms of secondary considerations, such as rate of data collection, cost, and complexity of the design.

**EXAMPLE 14A**

Referring further to the drawings, Figure 61A pictorially illustrates a method 340 for zooming in on a suspected pathological feature in a breast, as a process of two or more iterations, in accordance with embodiments of the present invention.

5 As seen in Figure 61A, the method 340 may be described, pictorially, as follows:

In I: The region-of-interest 200, associated with the organ 215, such as the breast 215, is defined for the body section 230.

10 In II: The model 250 of the volume U is provided for the region-of-interest 200, possibly with one or several of the modeled organ targets HS, and within the anatomical constraints AC, for obtaining the optimal set of views for the region-of-interest 200. The optimal set of views is then applied to the region-of-interest 200, encompassing the breast 215 of the body section 230.

15 In III: When the suspected organ target 213 is identified, in vivo, in the breast 215, by radioactive-emission measurements at the optimal set of views, a second, inner region-of-interest 200' is defined, encircling the suspected pathological feature.

20 In IV: A second model 250' of a second volume U' is provided for the second, inner region-of-interest 200', preferably, with at least one modeled organ target HS, simulating the suspected organ target 213, for obtaining an optimal pathology set of views for the second region-of-interest 200'. The second, pathology set of views is then applied to the second, inner region-of-interest 200' of the body section 230.

Alternatively, as seen in Figure 61B, the method 340 may be described, pictorially, as follows:

25 In I: The region-of-interest 200, associated with the organ 215, such as the breast 215, is defined for the body section 230, when compressed between two plates 902 and 904, for example, mammograph plates.

30 In II: The model 250 of the volume U is provided for the region-of-interest 200, possibly with one or several of the modeled organ targets HS, and within the anatomical constraints AC, representing the mammograph plates, for obtaining the optimal set of views for the region-of-interest 200. The optimal set of views is then applied to the region-of-interest 200, encompassing the organ 215 of the body section 230.

In III: When the suspected organ target 213 is identified, in vivo, in the organ 215, by radioactive-emission measurements at the optimal set of views, a second, inner region-of-interest 200' is defined, encircling the suspected organ target 213.

In IV: A second model 250' of a second volume U' is provided for the second, inner region-of-interest 200', preferably, with at least one modeled organ target HS, simulating the suspected organ target 213, for obtaining an optimal pathology set of views for the second region-of-interest 200'. The second, pathology set of views is then applied to the second, inner region-of-interest 200' of the body section 230.

It will be appreciated that this camera system may also be used as a PET.

Figures 61A – 61B schematically illustrate the modeling of a breast in accordance with embodiments of the present invention. However, generally the breast is tested when compressed, as described hereinbelow.

Mammography is currently the most effective method of screening for breast cancer, for the detection of early non-palpable tumors. In essence, it involves compressing the breast between two plates, a support plate and a compression plate, and passing x-rays through the compressed breast. The compression is desirous both in order to spread the breast fatty tissue thin, to reduce its attenuation, and in order to fix the breast tissue, with respect to a frame of reference, so that the x-ray image may be correlated with a surgical tool frame of reference, such as a biopsy needle frame of reference, for guiding the surgical tool to a suspected location on the x-ray image, without the breast tissue moving between the taking of the x-ray image and the guiding of the surgical tool.

Often stereotactic mammography is applied, meaning that the x-ray head is rotated with respect to the plates, so as to provide at least two views of the fixed breast, compressed between the plates, from at least two angles, for stereo imaging.

In general, each breast is imaged separately, generally, both in a vertical direction and from the side (laterally), preferably, stereotactically. In other words, generally, at least four views of each breast are taken, two vertically and two laterally.

A surgical instrument, for example, a biopsy needle, or an ablation device, such as a cryosurgery device, an ultrasound ablation device, a knife, or a laser ablation device, may be built onto the mammograph, its frame of reference correlated with that of the x-ray image.

Figure 62A schematically illustrates the basic mammograph 900, showing a structural support 929, which defines a frame of reference 80, and which includes a support plate 902 and a compression plate 904, the compression plate 904 being adapted for motion along an arrow 906, so as to compress a breast 909 on the support plate 902.

An x-ray tube 905 is preferably arranged so as to move within a track 907, for obtaining x-ray images of the compressed breast 909 from at least two views, so as to obtain stereotactic viewing, for depth evaluation. A film 901 is preferably arranged under the breast 909, for example, under the support plate 902, for registering the x-ray image.

Additionally, the mammograph 900 is preferably adapted for rotation, as illustrated by an arrow 908, for compressing a breast from at least two orientations, for example vertically and laterally.

A surgical tool 903, for example, a biopsy needle 903 or an ablation device 903, such as by cryosurgery or laser, or a knife 903, may be built onto the mammograph 900, its frame of reference correlated with the frame of reference 80, using position tracking devices or a linkage system, as known.

Figures 62B and 62C schematically illustrate a system 925 of an ultrasound imager 915, operative with the two plates 902 and 904, in accordance with embodiments of the present invention. The importance of performing ultrasound between two plates, as in the case of x-rays, is that the two plates fix the breast with respect to the frame of reference 80, and in fact, convert the breast to a rigid-like tissue, so that any suspicious findings can be located by the surgical tool 903.

In Figure 62B, the ultrasound imager 915 is arranged to slide along tracks 917, for example, on the compression plate 904, while a layer of gel 913 or hydrogel 913, between the compression plate 904 and the breast 909 ensures good contact for ultrasound imaging. In this manner, an ultrasound image, correlated to the frame of reference 80, when the breast is under compression, may be obtained.

Alternatively, as seen in Figure 62C the ultrasound imager 915 may be built onto the structural support 929, its frame of reference correlated with the frame of reference 80, using position tracking devices or a linkage system, as known.

Referring further to the drawings, Figures 63A – 63E schematically illustrate a radioactive-emission camera 1000 for the breast, for operation with the mammograph

900 of Figure 62A, or for operation with another system, wherein a breast is compressed between two plates, in accordance with embodiments of the present invention.

Figure 63A schematically illustrates an external appearance of the radioactive-emission camera 1000, for the breast. The camera 1000 has a driving portion 990 and an imaging portion 980, enclosed in a sheath 985. The imaging portion 980 defines cylindrical coordinates 987 of a longitudinal axis along the x-axis, and an r-axis, perpendicular to the longitudinal axis.

Figures 63B – 63C schematically illustrate an internal structure of the radioactive-emission camera 1000, for the breast. The imaging portion 980 includes several of the blocks 90, for example, between two and six of the blocks 90, arranged within the sheath 985. It will be appreciated that another number, which may be larger or smaller, and which may be odd or even, may be employed.

In Figure 63B, the motions experienced by the blocks 90 are illustrated with respect to the cylindrical coordinates 987 of x;r.

A first motion is a rotational motion of all the blocks 90, moving as a single body, with the shaft 85 and the internal structure 21, around the x-axis, in the direction between  $+\omega$  and  $-\omega$ , as illustrated by the arrow 52. The first motion is powered by the motor 88.

A second motion is an oscillatory motion of the individual blocks 90, powered by the secondary motor 86, the secondary shaft 84, and the motion transfer link 74, the motion transfer link 74 moving in a linear, sliding motion, as shown by the arrow 71.

At each orientation of the internal structure 21 with respect to  $\omega$ , around x, the second, oscillatory motion about r takes place, individually by each of the block 90, the oscillatory motion about r being between  $-\phi$  and  $+\phi$ , as illustrated by the arrow 50, and as taught hereinabove, with reference to Figures 20A – 20H.

Thus, the overall motion is as illustrated hereinabove, with reference to Figure 23C and Figure 20H.

Further as seen in Figure 63C, the rotational motion in the direction of the arrow 52 is provided by a motor 88 and the shaft 85, which together form the motion provider 76. The motor 88 may be an electric motor, for example, a servo motor. The oscillatory motion in the direction of the arrow 50 is provided by a secondary motor



86, a secondary shaft 84 and a motion transfer link 74. The secondary motor 86 may also be an electric motor, for example, a servo motor. The secondary motor 86, secondary shaft 84 and the motion transfer link 74, together, form the secondary motion provider 78, for the oscillatory motion, in the direction of the arrow 50.

5 Thus, for the radioactive-emission camera 1000, for the breast:

- i. The different blocks 90 provide views from different orientations; and
- ii. The different blocks 90 may change their view orientations independent of each other.

10 It is important to point out that during the operation of the camera 1000, the sheath 985 of the imaging portion 980 (Figures 63A and 63B) remains stationary, while the internal structure 21 (Figure 63C) rotates around the x-axis. The sheath 985 may be formed of a carbon fiber, a plastic, or another material, which is substantially transparent to nuclear radiation.

15 Figures 63D and 63E illustrate further the oscillatory motion of the blocks 90, within the sheath 985, as described by the arrows 50, by showing the blocks 90 at different positions, along their oscillatory travel. Figures 63D and 63E further illustrate a viewing side 986 and a back side 988 for the camera 1000.

20 Referring further to the drawings, Figures 64A – 64M schematically illustrate systems 910, which include the radioactive-emission cameras 1000 for the breast, operating with systems, in which a breast is compressed between two plates, for example, as in the mammograph 900, in accordance with embodiments of the present invention.

25 Preferably, as seen in Figures 64A and 64B, the cameras 1000 are mounted onto the two plates, the compression plate 904, and the support plate 902, such that their viewing sides 986 face each other. Preferably, the cameras 1000 are aligned with the x-axis, as seen. Alternatively, the cameras 1000 may be aligned with the y-axis. It will be appreciated that the cameras 1000 may be mounted only on one plate, the compression plate 904 or the support plate 902.

30 Additionally, as seen in Figure 64C, one or several of the cameras 1000 may be mounted as edge cameras, for positioning at edges 992 and 994, supplementing the cameras 1000 mounted on the plates, for obtaining views from the sides of the compressed breast.

An alternative embodiment is illustrated in Figure 64D, wherein a single one of the cameras 1000 may be mounted on each of the plates 902 and 904, the camera 1000 being adapted for travel along a track 914, in a direction of an arrow 918, by a dedicated motion provider 916, thus providing the views that a plurality of the cameras 1000 would have provided, as illustrated in Figures 64A – 64B.

It will be appreciated that edge cameras 1000, may be added to the embodiment of Figure 64D, in a manner similar to that of Figure 64C.

Figure 64E schematically illustrates a control unit 890, for controlling the motions of the blocks 90 (or the detecting units 12, when not arranged in blocks) of the cameras 1000 and for analyzing the measurements and constructing the images. Preferably, a single control unit is used both for the x-ray imager, or the ultrasound imager 915, on the one hand, and the radioactive-emission cameras 1000, on the other. Alternatively, individual control units may be used, one for each modality. Alternatively, the system 910 for the breast is provided with a storage device 892, such as a CD or a disk, which contains the software for operating the system 910 for the breast with an existing computer on the site. It will be appreciated that the control unit 890 may be a PC, a laptop, a palmtop, a computer station operating with a network, or any other computer as known.

In accordance with embodiments of the present invention, frames may be provided for mounting the radioactive-emission cameras 1000 on the plates 902 and 904.

As seen in Figure 64F, a frame 912 may be provided for either the support plate 902 or the compression plate 904, designed for accepting the cameras 1000 lengthwise, by inserting the cameras 1000 in holes 926.

Alternatively, as seen in Figure 64G, the frame 912 may be designed for accepting the cameras 1000 widthwise.

Additionally, as seen in Figure 64H, a frame 922 is designed for accepting the cameras 1000 widthwise or lengthwise, wherein the frame 922 further includes an edge section 924, for supporting the edge cameras of Figure 64C.

Furthermore, as seen in Figure 64I, two complementary frames may be provided, one designed as the frame 922, for accepting the cameras 1000 lengthwise (or widthwise) along the plate and for accepting the edge cameras, as illustrated in

Figure 64H, and the other, designed as the frame 912, for accepting the cameras 1000 lengthwise (or widthwise) along the plate.

As seen in Figure 64J, a frame 923 may be designed for accepting a single one of the cameras 1000, lengthwise, adapted for sliding widthwise along the plate, in a channel 928, by the dedicated motion provider 916. Alternatively, the frame 923 may be designed for accepting the camera 1000 widthwise, adapted for sliding lengthwise.

As seen in Figure 64K, a frame 927 may be designed for accepting a single one of the cameras 1000, for example, lengthwise, adapted for sliding widthwise along the plate, in a channel 928, by the dedicated motion provider 916, wherein the frame 927 further includes the edge section 924, for supporting the edge camera 1000 of Figure 64C.

In accordance with embodiments of the present invention, nuclear imaging by radioactive-emissions, co-registered with x-ray mammography, may be obtained by a method 1010, illustrated in Figure 64L, in flowchart form, as follows:

- in a box 1012: the breast is compressed between the plates;
- in a box 1014: an x-ray mammography is performed, as seen in Figure 62A, preferably from at least two orientations of the x-ray tube 905;
- in a box 1016: the cameras 1000 are mounted on the plates, and radioactive-emission measurements are performed;
- in a box 1018: where necessary, the surgical tool 903 may be employed, while the breast is still compressed between the two plates.

It will be appreciated that the order of the steps of boxes 1014 and 1016 may be reversed.

Preferably, the images of the x-ray mammography and the nuclear imaging are co-registered and analyzed together.

However, it will be appreciated that only nuclear imaging by radioactive-emission measurements may be performed, without x-ray imaging.

Where ultrasound imaging co-registered with nuclear imaging by radioactive-emissions is desired, a method 1020, illustrated in Figure 64M, in flowchart form, applies, as follows:

- in a box 1022: a hydrogel layer is placed between one of the plates, for example, the compression plate 904 and the breast, or a gel is spread over the breast, so as to serve as an ultrasound interface between the plate and the breast;

in a box 1024: the breast is compressed between the plates;

in a box 1026: the cameras 1000 are mounted on the plates, and radioactive-emission measurements are performed;

in a box 1028: the cameras 1000 are replaced by an ultrasound imager, for example as illustrated in Figures 62B or 62C, and ultrasound imaging is performed;

in a box 1030: where necessary, the surgical tool 903 may be employed, while the breast is still compressed between the two plates.

It will be appreciated that the order of the steps 1026 and 1028 may be reversed.

Preferably, the images of the x-ray mammography and the nuclear imaging are co-registered and analyzed together.

Referring further to the drawings, Figures 65A – 65C schematically illustrate a radioactive-emission camera 930, for imaging a breast under vacuum, in accordance with another preferred embodiment of the present invention.

As seen in Figure 65A, the camera 930 includes a vacuum cup 934, shaped as a cone and connected to a vacuum system 932, for creating a vacuum in a cavity 935 within. The vacuum in the cavity is used both to stretch the breast so as to spread the fatty tissue thin and to fix the breast tissue with respect to a frame of reference, so a surgical device may be employed, where needed, while the breast tissue remains fixed in place.

A vacuum ring 936, for example of natural or synthetic rubber, helps maintain the vacuum in the cup 934.

The vacuum cup 934 defines the frame of reference 80 and a plurality of the blocks 90 are arranged along the walls 938 of the suction cup 934, each adapted for at least one, and preferably two rotational motions, for example, as illustrated with reference to Figures 22I – 22M and Figures 22Q – 22R, or Figures 22N – 22P, for imaging a breast in the cavity 935. Alternatively, the blocks 90 may be arranged in the assemblies 92, as illustrated with reference to Figures 22A – 22H.

A surgical tool may be attached to the camera 930, and correlated to its frame of reference, for example as taught with reference to Figure 62B.

The motions of the blocks 90 are preferably automatic, controlled by the control unit 890 (Figure 64C).

Preferably, the inner walls 938 of the cup 934 are substantially transparent to radioactive emission.

Figure 65B schematically illustrates an embodiment wherein a vacuum cylinder 934 is used in place of a conical cup, and the blocks 90 are arranged in assemblies 92, for example, as illustrated with reference to Figures 16E and 24A – 24H.

Figure 65C schematically illustrates an embodiment wherein the vacuum cylinder 934 is used, and a single one of the assemblies 92 is arranged for traveling around the cylinder 934, in the direction of an arrow 940, by a motion provider 942.

Referring further to the drawings, Figures 66A – 66F schematically illustrate a radioactive-emission camera 950, for imaging the breasts in the natural state, in accordance with another preferred embodiment of the present invention.

As seen in Figure 66A, the radioactive-emission camera 950, for imaging the breasts in a natural state, is designed as an extracorporeal unit which may be positioned against the breasts, operating as taught with reference to any one of Figures 20A – 22R. Preferably, the radioactive-emission camera 950, for imaging the breasts is attached to a gantry 952, which may provide adjustments as seen by arrows 954 and 956.

Additionally, the patient may be positioned on a chair 960, as seen in figure 66B.

The control unit 890 may be used for controlling the motions of the blocks 90 (Figures 22A – 22H or 22I – 22R) or the detecting units 12, when not arranged in blocks, and for analyzing the measurements and constructing the images. Alternatively, the radioactive-emission camera 910 for the breast is supplied with a storage device 892, which contains the software for operating the radioactive-emission camera 910 for the breast with an existing computer on the site. It will be appreciated that the control unit 890 may be a PC, a laptop, a palmtop, a computer station operating with a network, or any other computer as known.

Figure 66D schematically illustrates a woman 970 being examined by the radioactive-emission camera 950, when seated on the chair 960. It will be appreciated that the examination may also be conducted when the woman 970 is standing or lying on a bed.

Figure 66E schematically illustrates the inner structure radioactive-emission camera 950 in accordance with a preferred embodiment of the present invention. Figure 66E shows the overall structure 20, the parallel lines of assemblies 92, possibly of an even number, each with a dedicated motion provider 76 and a dedicated secondary motion provider 78, and the rows of blocks 90, possibly arranged in pairs, along the assemblies 92.

The camera 950 defines the frame of reference 80, while each assembly 92 has a reference cylindrical coordinate system of  $x;r$ , with rotation around  $x$  denoted by the arrow 62 and oscillatory motion about  $r$ , denoted by the arrow 50.

Figure 66F schematically illustrates the model 250 of the two breasts, modeled as the volumes  $U$ , and the anatomical constraints associated with them, for determining an optimal set of views for radioactive-emission measurements.

It will be appreciated that imaging, in accordance with embodiments of the present invention relates to the imaging of the whole breast, or to a portion of the breast, the armpits near the breasts, (and) or the two breasts.

Preferably, the radiopharmaceuticals associated with the radioactive-emission camera for the breast may be Tc-99m bound to Sestamibi, a small protein molecule, made for example, by Bristol Myers Squibb, and marketed as Miraluma, used widely for breast cancer detection.

The present invention applies to detecting and differentiating between various types of breast disorders, for example as illustrated in Figure 66G, hereinabove, as follows.

- i. fibroadenomas 8, which are fibrous, benign growths in breast tissue.
- ii. cysts 9, which are fluid-filled sacs and may disappear sometimes by themselves, or a doctor may draw out the fluid with a needle.
- iii. a breast abscess 11, which is a collection of pus, resulting from an infection.
- iv. fibrocystic breast disease 13, which is a common condition characterized by an increase in the fibrous and glandular tissues in the breasts, resulting in small, nodular cysts, noncancerous lumpiness, and tenderness, wherein treatment of the cysts may be all that is needed.
- v. a tumor 15, which may be precancerous or cancerous, and which usually shows up as a white area on a mammogram even before it can be felt. In cases



where the tumor 15 is cancerous, it may appear as a white area with radiating arms. A cancerous tumor 15 may have no symptoms or may cause swelling, tenderness, discharge from the nipple 4, indentation of the nipple 4, or a dimpled appearance 17 in the skin over the tumor.

5        Additionally, the present invention applies to detecting various types of breast cancers, such as:

- i.        ductal cancer, which affects the cells of the ducts;
  - ii.       lobular cancer, which begins in the lobes or lobules of the breast; and
  - iii.       inflammatory breast cancer, which is an uncommon type of breast
- 10       cancer and causes the breast to be warm, red, and swollen.

It will be appreciated that the present invention further applies to other types breast disorders, which may be cancerous, precancerous, or benign.

Additionally or alternatively, the present invention applies to secondary breast cancer, for example, originating from the lungs, or other parts of the body.

15       Furthermore, the radioactive-emission camera for the breast may be designed for and used on a single breast or designed for and used simultaneously on the two breasts.

It will be appreciated that although breast cancer in men and children is rare, the present invention may be used for the detection of breast cancer in men and

20       children as well.

### **Overall Camera Performance**

The following section reviews the overall camera performance for different camera designs and illustrates configurations which conform to body contours, so as

25       to be as close as possible to the anatomical constraints (Figure 5B). Additionally, the importance of distance between the organ target 213 and the detecting block 90 is explained. The camera performance is considered with respect to the following:

- i.        detecting efficiency;
- ii.       acquisition time;
- 30       iii.       spatial resolution;
- iv.       wasteful viewing, in regard to ordinary gamma cameras;
- v.        adjustable design;
- vi.       independent viewing by each block or detecting unit;

- vii. criteria for camera design;
- viii. experimental results.

### **i. Detecting Efficiency**

Referring further to the drawings, Figures 67A and 67B schematically illustrate the solid angle by which the radiation emission source 213 "sees" the detecting block 90. At a distance of  $R_1$ , the solid angle is  $\beta_1$  and at the distance of  $R_2$ , the solid angle is  $\beta_2$ , wherein an inverse relation exists between  $R_1$  and  $R_2$  and  $\beta_1$  and  $\beta_2$ , such that when  $R_2 > R_1$  then  $\beta_1 > \beta_2$ .

Furthermore, for the detecting block 90 of an area  $\pi r^2$ , at a distance  $R$  from a point source, the detecting efficiency is a function of the ratio of the detecting area  $\pi r^2$  to the area of the sphere  $4\pi R^2$ , so as to behave as a function of  $r^2/R^2$ . Thus, for the detecting block 90 of a fixed detecting area, as the distance  $R$  from the source 213 increases, the detecting efficiency decreases, proportionally to  $R^2$ .

It will be appreciated that a similar analysis is valid for the detecting unit 12, on a pixel basis, as well.

### **ii. Acquisition Time**

A related issue is the acquisition time, for statistically meaningful results. Radioactive emission may be described by the Poisson distribution, for which the counting error for  $N$  counts is described by  $N^{1/2}$ . For example, when 10,000 counts have been detected, the counting error is  $10,000^{1/2}$ , or 100, which is 1% of  $N$ . Where it is desired to obtain data at a predetermined level of accuracy, a minimal level of counts must be obtained. Thus, for an accuracy level of 1%, 10,000 counts must be obtained; for an accuracy level of 0.1%, 1,000,000 counts must be obtained, and so on.

Yet, when the distance  $R$  between the source 213 and the detecting block 90 is increased, the counting efficiency falls proportionally to  $R^2$  and the number of counts per minutes falls proportionally to  $R^2$ , and so the acquisition time required to reach a predetermined number of counts, for a predetermined accuracy level, increases proportionally to  $R^2$ .

### **iii. Spatial Resolution**

Referring further to the drawings, Figures 68A – 68B schematically illustrate the effect of the distance R on the spatial resolution.

As seen in Figure 68A, the organ target 213 has a radius q, which may be, for example, of the order of magnitude of the radius r of the detecting block 90, so that  $q \sim r$ . The organ target 213 may have a distribution of activity, for example, a high-level portion 213A, a medium-level radiation portion 213B, and a relatively low-level radiation portion 213C.

As seen in Figure 68B, given, for example, a 3 X 3 pixel arrangement and a collection angle  $\beta$ , when the block 90 is very close to the organ target 213, such that R1 is substantially zero, and given that  $q \sim r$ , the organ target 213 is viewed by practically all the 3 X 3 pixels, resulting in a high-resolution image.

As seen in Figure 68C, at a distance R2, the organ target 213 is barely viewed by more than one pixel, resulting in a low-resolution image.

As seen in Figure 68D, at a distance R3, the organ target 213 is viewed by less than one pixel, resulting in a very low-resolution image.

Thus, the number of pixels in the block 90 provides for a spatial resolution capability. In order for this resolution capability to be realized, however, the distance between the detecting block 90 and the organ target 213 should be as small as possible.

#### **iv. Wasteful Viewing, in Regard to Ordinary Gamma Cameras**

Referring further to the drawings, Figures 69A – 69D schematically illustrate different view arrangements.

Figure 69A illustrates four blocks 90A, 90B, 90C, and 90D for viewing the organ target 213, the blocks arranged around the body section 230. The block 90A, at the distance R1 from the organ target 213, is as close as possible to the external surface of the body section 230, such that it is substantially touching it. Therefore, the block 90A is at an optimal viewing position for the organ target 213. The block 90B is at a distance R2 from the organ target 213, where  $R2 > R1$ , but it is still in position to view the target 213, from that distance. Therefore, the block 90B is at a suboptimal position for viewing the organ target 213. The block 90C does not view the organ target 213, yet it does view the body section 230, so it may also be considered at a suboptimal position. The block 90D does not view the body section 230, so the view

of the block 90D is wasteful, in that it does not provide any information regarding the body section 230.

As Figure 69A illustrates, blocks which substantially touch the surface of the body section 230 will always provide some information about it. Yet blocks 90 that are distant from the body section 230 may view areas altogether outside the body section 230, so their contribution is wasteful.

This point is further illustrated in Figures 69B – 69D, which illustrate the use of a rigid camera of the prior art, for example, as taught by US Patents 6,597,940 and 6,671,541, both to Bishop et al. As may be understood from Figure 69B-C, as the blocks 90A and 90B are brought into close proximity with the body section 230, blocks 90C, 90D, 90E and 90F are moved away from it, and their views become suboptimal or even wasteful. Conversely, as the blocks 90F and 90E are brought into close proximity with the body section 230, blocks 90D, 90C, 90B and 90A are moved away from it, and their views become suboptimal or even wasteful

Similarly, as the blocks 90B, 90C, and 90D are brought into close proximity with the body section 230, the views of blocks 90F and 90A become suboptimal or even wasteful

#### **v. Adjustable designs**

Referring further to the drawings, Figure 71 schematically illustrates an adjustable PET camera 1150, in accordance with embodiments of the present invention. The PET camera 1150 is formed of a plurality of the blocks 90, placed substantially on the body section 230. Such a camera, when completely surrounding the body section 230, essentially sees all coincident emissions coming out of the body, and greatly increases the counting efficiency for PET.

Referring further to the drawings, Figures 72A – 72E schematically illustrate adjustable cameras 1160 and 1170A-B mounted on adjustable overall structures, for conforming to contours of the body section 230, in accordance with embodiments of the present invention.

As seen in Figures 72A – 72B, the cameras 1160 and 1170A-B include hinges 90X between the blocks 90, such that the positions of the blocks may be adjusted. Alternatively, as seen in Figure 72C, several blocks 90 may be arranged in a row to form an assembly 92 and the camera may include hinges 90X between the assemblies

92, such that assemblies 92 may be adjusted. Figure 72A illustrates the camera 1160 prior to the adjustment, and Figure 72B illustrates the camera 1160 after adjustment. Figure 72C illustrates the camera 1170, as may be used for coincident imaging or another whole body imaging.

5        Figure 72D schematically illustrates the viewing range of the camera 1160, in accordance with the present embodiment.

Figure 72E schematically illustrates a pictorial view of the camera 1160, of the present embodiment.

Referring further to the drawings, Figures 73A – 73B schematically illustrate  
10        adjustable cameras 1100, in accordance with another embodiment of the present invention.

Figure 73A illustrates the blocks 90 mounted on a flexible structure 1180 such as cloth, vinyl or the like. Each assembly 90 preferably includes a position tracking device 1116 and at least one but preferably two or more motion providers, such as  
15        motion providers 1114 and 1112, to provide the assembly 90 with at least one, but preferably two, three, or possibly up to six degrees of motion.

Figure 73B illustrates the blocks 90 linked by chains 1120, to provide the adjustable character.

It will be appreciated that the position tracking device may be magnetic,  
20        electromagnetic, optical, or another device, as known. For example, each block 90 may include a Minibird<sup>TM</sup>. Alternatively, two cameras may track the position of each block 90. Alternatively, other tracking methods may be used.

Referring further to the drawings, Figures 74A – 74B schematically illustrate adjustable cameras 1200, in accordance with still another embodiment of the present  
25        invention. The cameras 1200 are constructed as detecting modules 1216, which contain blocks 90 or detecting units 12, the detecting modules 1216 being arranged on tracks 1212 which are associated with a coordinate system 1214. Each of the detecting modules 1216 includes an encoder 1218, operative as the position tracking device 124 (Figures 2 and 3A), as known. The modules move along the tracks 1212  
30        by means of a motion provider (not shown) while sending information regarding their coordinates together with measurements taken to the data-processing system 126 (Figures 2 and 3A).

**vi. Independent Viewing by Each Block or Detecting Unit**

In accordance with embodiments of the present invention, each block 90 of the adjustable camera construction (Figures 71 – 73B) or each detecting unit 12, where single-pixel detecting units 12 are used, may be provided with at least one, and preferably, two, three, or as many as six degrees of motion such as, for example, rotational motion around the x, y, and z, axis, oscillatory motion about these axes, or translational motion along these axes. In this manner, each block 90 may be preprogrammed to view each portion of the body section 230, in accordance with some predetermined schedule. For example, one of the blocks 90 may perform oscillatory motion, while an adjacent one of the blocks 90 may perform rotational motion. Thus, areas that are known to pose little susceptibility to abnormalities may be viewed differently from areas that are more susceptible to abnormalities. Additionally, active vision may take place. For example, where something suspicious is viewed, a decision to view it for a longer period of time and to thus obtain better data may be made by the data-processing system 126 (Figure 2), so that the associated blocks 90 may be instructed to view an area longer. Alternatively, where not enough data has been acquired for the desired level of accuracy, more data may be collected, i.e., the number of counts may be increased so as to reduce the margin or error to 1%.. In other words, when using multiple, independent blocks 90 or detecting units 12, each may spend more time in one region than in another, and each may spend the time needed to reach a desired level of accuracy. Thus, one block or detector may spend a long time (within a predetermined limit) in one region, while another may spend less time and move on to another angle and position so as to provide a new view. Similarly, one block 90 or detecting unit 12 may use large steps, while another may use fine steps.

The present invention relates to situations that are unlike current systems, where the detecting units or blocks are fixed, with respect to each other, so individual optimization by block or by detecting unit is not possible.

The reverse is also possible, and a decision to obtain data for less than originally intended may be made. Also, cursory imaging may be performed and, where necessary, a decision may be made to acquire more data. It will be noted that the blocks along the camera may be designed differently and may include different



collimators, for the different portions of the body section 230, such as those taught with reference to Figures 17C – 17F. . For example, the blocks 90 at the edge may have wide-angle collimators and those that are in the central portion of the blocks 90 may have narrow collimators.

5

### **vii. Criteria for Camera Design**

An overall camera design may be based on the following criteria:

i. a distance from the surface of the body section 230 to the detecting unit 12 or the block 90 which is no greater than 5 cm and, preferably, no greater than 3 cm, and, more preferably, no greater than 2 cm.

10

ii. wasteful viewing for less than 50% of the viewing of each detecting unit 12 or block 90 and, preferably, less than 30% of the viewing time and, more preferably, less than 20 % of the viewing time.

iii. Substantially no detecting unit 12 or block 90 is positioned so as not to view the body structure at all.

15

iv. a collimator solid collection angle of at least 0.0005 steradians, or at least 0.001 steradians, or at least 0.003 steradians, or at least 0.005 steradians, or at least 0.01 steradians, or at least 0.03 steradians, or at least 0.05 steradians, or at least 0.08 steradians.

v. alternatively, a collimator collection solid angle which is configured to view substantially a whole organ, such as a heart, or substantially a large portion of the organ.

20

vi. a block size along the rotational axis, for the block 90, of less than 10 cm and, preferably, of less than 6 cm and, more preferably, of less than 2 mm.

vii. independent motion control for each of the blocks 90, along at least one rotational axis, preferably along at least two rotational axes and, more preferably, along the three rotational axes and the three translational axes.

25

Wherein a portion of these or all of these may be incorporated into the camera design.

30

### **viii. Experimental Results**

Referring to the drawings Figures 75A and 75B illustrate Teboroxime physiological behavior, according to Garcia et al. (Am. J. Cardiol. 51<sup>st</sup> Annual Scientific Session, 2002).

Referring further to the drawings, Figures 76A – 80D illustrate experimental results of the camera of the present invention and results of a conventional gamma camera, in terms of resolution, speed, and contrast. In all the experiments, the detectors used were 16x16 pixilated (2.54x2.54 mm in size) CZT arrays made by Imarad, Rehovot, Israel and driven by the XA controller system made by IDEAS asa., Norway.

#### Test No 1: Speed and Resolution

Performances of the camera of the present invention and of the conventional gamma camera were compared by equivalent setups, as follows:

For the camera of the present invention, a center of viewing was at a distance of 150 mm from the collimators' distal end with respect to an operator. A 5 mili Curie Cobalt 57 line source was placed at a distance of 1 cm from the center of viewing, so as to be off center for the viewing. A total of 13.5 million photon counts were taken. Acquisition time was 49 seconds.

For the conventional gamma camera, a center of rotation was at a distance of 150 mm from the collimators' distal end with respect to an operator. A 5 mili Curie Cobalt 57 line source was placed at a distance of 1 cm from the center of rotation, so as to be off center for the rotation, and the same number of counts, 13.5 million photon counts, was taken. Acquisition time was 600 seconds.

Thus, the camera of the present invention was about 12 times more sensitive than the conventional gamma camera.

The image of the source was reconstructed using dedicated reconstruction algorithms based on the EM method and developed by the inventors. The reconstruction algorithms used on the conventional unit were OSEM/MLEM based.

Figure 76A represents results with the camera of the present invention.

Figure 76B represents results of the conventional gamma camera.

The measured FWHM (Full Width at Half Maximum) resolutions are shown as follows:

	354
System/Reconstruction	Resolution FWHM (NEMA) [mm]
camera of the present invention	5.5
conventional gamma camera	10.4

#### Test No. 2: Resolution as a Function of Scattering Distance

A standard NEMA cylindrical phantom was filled with water, and a 5 mil Curie Cobalt 57 line source of 190 mm in length and 1 mm in diameter was placed at its center, as illustrated in Figure 76C. The cylindrical phantom was placed at a distance R from the distal end of the cameras' collimators. Reconstruction images from two 40-second acquisitions were performed and analyzed, wherein the first acquisition was based on equal angle span for all views (Fixed Angle Spans), and the second acquisition was based on adjusted angle viewing, for viewing equal sectors of the region-of-interest (Fixed ROI).

For image reconstruction, a maximal intensity projection (MIP) of the reconstruction without attenuation correction is given in Figure 76D, based on the combined total of the two acquisitions. The x-z and the y-z planes each show the line source as a line, and the x-y plane provides a cross-sectional view of the line.

Figure 76E illustrates the reconstructed cross-sectional intensity of the line source for the fixed scan angle and Fixed ROI cases, respectively, and for varying distances R from the camera. As expected, the FWHM increases with increasing R.

Figures 76F and 76G schematically show NEMA resolutions in the x and y directions, respectively, for the fixed-angle span acquisition, while Figures 76H and 76I schematically show NEMA resolutions in the x and y directions, respectively, for the fixed-ROI acquisition.

#### Test No. 3: NEMA Three Line Source Acquisition

Three Cobalt 57 line sources were placed inside a standard NEMA phantom, as seen in Figure 77A.

Viewing coverage was 200 degrees, wherein the distance from the distal end of the collimators to the center of viewing was 150 mm. The total net acquisition time was 60 seconds. The images shown in Figures 77B - 77D are based on raw reconstruction, without attenuation correction or smoothing.

After application of a simplistic, model-based attenuation correction, which is acceptable in the case of water as the scattering and absorbing medium and circular symmetry of an object, the results are shown in Figures 77E – 77G.

Table 89 below provides resolution numbers for the pre- and post-attenuation correction results, as follows:

Table 89

<b>Without Attenuation Correction</b>	<b><i>NEMA resolution FWHM [mm]</i></b>		
	<b><i>Point #1</i></b>	<b><i>Point #2 (Center)</i></b>	<b><i>Point #3</i></b>
X- Direction	5.6	7.7	4.4
Y-Direction	5.4	7	4.4
<b>With Attenuation Correction</b>	<b><i>NEMA resolution FWHM [mm]</i></b>		
	<b><i>Point #1</i></b>	<b><i>Point #2 (Center)</i></b>	<b><i>Point #3</i></b>
X –Direction	6.1	7.6	3.9
Y-Direction	6.3	7.6	4

#### Test No. 4: Resolution, Acquisition Time, and Contrast

As shown in Figures 78A - 78C, two sources, A and B, were placed in a cylindrical Perspex phantom, designed to allow the insertion of sources of different sizes and intensities.

A comparison of radioactive-emission imaging of the camera of the present invention and of a conventional gamma camera was made, and this included image evaluation, sensitivities, and contrast differences.

The cylindrical Perspex phantom was placed with its center at the center of viewing of the camera. The distance from the distal end of the collimators to the center of the phantom cylinder was 100 cm.

The total radiation coming from the cylinder, including radiation from background, insert A, and insert B, was 930 $\mu$ Ci of Tc-99m. The ratio of the amount of radiation from insert A to background radiation was 2:1, while that of radiation from insert B to background radiation was 3:1. Acquisition time was 40 seconds and

1.4 million counts were acquired. The reconstructed images are seen in Figures 79A – 79C. Both the 2:1 and 3:1 Target to Background ratio targets are visible.

The resulting measured contrasts are 2.6:1 and 1.6:1 for the 3:1 and 2:1 input contrasts, respectively, in the case of the camera of the present invention.

5        Figure 79D represents the reconstructed results using the conventional camera, for which the acquisition time to reach the 1.4 million counts was 20 minutes. The 3:1 target was reconstructed as a 1.3:1 ratio while the 2:1 target was indistinguishable from the background radiation. The main reason for this loss of contrast is the poor spatial resolution of the conventional camera when compared to that of the camera of  
10      the present invention.

#### Test No. 5: Reconstruction of Complex Objects - Torso Phantom Acquisition

A standard torso phantom of Anthropomorphic Torso Phantom Model ECT/TOR/P, produced by Data Spectrum Corporation, USA, was provided, as seen in  
15      Figure 80A.

The radioisotope Tc-99m was used as the tracer. The activity of the various organs was: Cardio - 0.5mCi, Background - 2mCi (0.19mCi/liter) and Liver - 0.23mCi (0.19mCi/liter).

20      An acquisition time of 1.25 minutes was used for the camera of the present invention, and an acquisition time of 12.5 minutes was used for the conventional camera. In both cases, 2.5 M counts were obtained.

Figure 80B illustrates the results using the camera of the present invention, and

Figure 80C illustrates the results using the conventional gamma camera.

25      The sensitivity ratio was thus 10:1. The reconstruction is visibly better in the case of the camera of the current invention.

Figure 80D illustrates a reconstructed three-dimensional image of the heart, from the phantom, using the camera of the present invention.

30      A cold area of 1 cm x 1 cm x 0.5 cm at a left side of the heart is clearly seen. Other cold areas are similarly visible.

#### Test No. 6: Sensitivity Studies

In another exemplary embodiment of the current invention, the

probe system includes multiple blocks of detectors positioned in a structure encircling the imaged area, each is able to rotate about a longitudinal axis substantially parallel to the main axis of the subject.

In a further example case of 10 such blocks of detectors, each covering a 40x160mm section covering about 180-200 deg of the circle around the imaged area, with 10 blocks of collimators each covering 1024 pixels arranged in a 16x64 pixel matrix, with square collimator opening of 2.46x2.46mm, and a length of 20mm], the system demonstrated ability to detect about one out of 1500 of the emitted photons from a 2.7mCi  $\text{Co}^{57}$  point source that was moved about in a 40x30x15cm volume facing the probe.

When located in the center of the imaged area (about 150mm from the detectors), while the energy window for acquisition was about 5%, and the detectors were sweeping a wide angular range.

In a further exemplary embodiment, substantially all detectors are able to simultaneously image the region of interest containing the point source and thus obtaining one out of every 500 of the emitted photons.

It is known to the skilled in the art that further opening the energy window of the detector to about 15%, enables acquisition of about one out of 250 photons of the photons emission in an experimental setting similar to the previous example.

In a further example, each such detector having multiple pixels is of about 5cm wide or more, thus producing a region of interest of at least 5cm in diameter, from which said sensitivity and said resolution is being obtained even without the need to move any of the detectors.

In a further possible embodiment of the present invention the width of each detector is about 10cm wide, thus enabling regions of interest of even bigger diameters at said resolution and sensitivity with a smaller detector motion such that bigger objects are continuously viewed by the detector with only small angular detector motion.

In a further possible embodiment of the present invention the detectors array may encircle the imaged subject to the extent of 360 deg, for example by having two hemi circles from both sides of the subject. The sensitivity in such case is estimated be about 1 in 125.



In a further exemplary embodiment additional detectors may be positioned to obtain views not perpendicular to the subject's main longitudinal axis, for example by upper view (e.g. from the shoulders) and abdominal view of the target region (in the case of cardiac mapping). It is estimated that such addition may increase the sensitivity but a factor of about x2.

As a result, an example embodiment of the present invention is estimated to be able to image a volume of about 5cm diameter located about 150mm from the detectors, with energy window of 15%, producing spatial resolution of about 5mm in approximately 100sec, with a total sensitivity of about 1 photons being detected out of 65 emitted.

It will be recognized by a person skilled in the art that a system built around the principles of this invention can thus reach the sensitivity necessary to detect substantially more than one photon from every 100 emitted. This result for an imaging system provides more than 100 time better sensitivity than commercially available cameras that have a sensitivity ranging from substantially from 170 counts/microCurie/minute (or 1 photon in 8500 photons emitted for a Low resolution low energy collimator to about 1 photon in every 15000 emitted for a high resolution medium energy collimator) , while maintaining similar energy windows, and potentially similar or better resolution.

#### Test No. 7: Sensitivity Studies - Grid Point Source

In a further experiment a  $\text{Co}^{57}$  point source of 2.7mCi activity was used in order to measure the sensitivity, resolution and geometric accuracy of the probe. A probe composed out of 10 detector columns, each containing detector pixels in a 16x64 pixel arrangement, where each pixel element had a dimension of 2.46x2.46mm and being covered by a Tungsten collimator matrix with .2mm septal thickness and 20mm septal length was used to image the point source. The energy window was set at 5% FWHM (6KeV total). A robotic arm was used to move the point source within a 40x30x15 cm rectangular volume at positions shown in Figure 70A. Figure 70B is a diagram showing the error of the reconstructed position relative to the nominal position as placed by the robot. It is evident that the deviation in position is less than 1mm for most points and less than 2.5 mm for all points. Fig 70C shows the FWHM diameter and the FWTM (Full Width Tenth Maximum) diameter for all points in the

volume. It is noted that the resolutions measured according to the NEMA standards are substantially under 10mm throughout the volume and do not exceed 15mm for all points, a performance equal to or superior to existing nuclear cameras for similar fields of View. The total net acquisition time for each point was 120 seconds and the typical count rate for most points (with the exception of positions that could not be viewed by all columns due to mechanical limitations), and the collected number of photons was substantially 7-8million counts for most positions fully viewed, yielding a sensitivity of 1 photon out of 1500 emitted in the energy window of 5%.

### ELECTRICAL SCHEME

Figure 143 describes an example of a system that includes multiple detection, amplification and signal processing paths, thereby avoiding saturation due to single hot source in space. Gamma-Ray photon (A) is hitting a pixelized CZT crystal. A hit is named 'Event'. The crystal is part of a 'CZT MODULE' (B) containing the CZT crystal divided into 256 pixels and 2 ASICS each receiving events from 128 pixels. The ASIC is OMS 'XAIM3.4' made by Orbotech Medical Systems, Rehovot, Israel, together with the CZT crystal. The 2 ASICs share a common output and transmit the data to 'ADC PCB' (C) that handles in parallel 4 'CZT MODULES'. Thus, a total of 1024 pixels are presently channeled through one ADC board. The system is capable of further increasing the accepted event rate by channeling every 2 ASICs through a single ADC. The 'ADC PCB' transmits the data to the 'NRG PCB' (D) that handles in parallel 10 'ADC PCBs', but could be further replicated should one want to further decrease "dead time". The 'NRG PCB' transmits the data to the 'PC' (E) where it is stored.

All in all, in the present embodiment, 40 'CZT MODULE' containing a total of 10240 pixels are transmitting in parallel to the PC.

The bottle neck, and hence the only constraint, of the system data flow is the ASICS in the 'CZT MODULE' and its connection to the 'ADC PCB':

1. An ASIC (128 pixels) can process only one photon hit within 3.5uSec, or 285,000 events/sec over 128 pixels, i.e. over 2200 events/px/sec-an exceedingly high rate.

2. 2 ASICS share the same output, and hence coincident event output of the 2 ASICS in a 'CZT MODULE' will cause a collision and information loss. The duration of an event output from the ASIC is 1uSec.

## 5           **GENERAL DESIGNS OF DETECTING UNITS, BLOCKS, ASSEMBLIES AND CAMERAS**

Referring further to the drawings, Figures 17A – 17H schematically illustrate detecting units 12 and blocks 90 that may be considered for possible camera designs.

Figures 17A and 17B schematically illustrate side and top views, respectively,  
10 of the basic detecting unit 12 (see also Figure 1A), having a detector 91 and a collimator 96, formed as a tube, of a collection angle  $\delta 1$ .

Figures 17C and 17D schematically illustrate side and top views, respectively, of the detecting unit 12, with the collimator 96 formed as a wide angle collimator, of a collection angle  $\delta 2$ .

15           Figures 17E and 17F schematically illustrate side and top views, respectively, of the block 90 (see also Figure 1B) of the detecting units 12, with the collimator 96 formed as a grid, and each of the detecting unit 12 having a collection angle  $\delta 3$ . As few as two or four, and as many as a hundred or several hundred of the detecting units 12 may be included in the block 90.

20           Figures 17G and 17H schematically illustrate side and top views, respectively, of the block 90 of the detecting units 12, with the collimator 96 formed as a grid, with two sizes of the detecting units 12, as follows: small detecting units 94A, of collection angles  $\delta 4$ , at the center of the grid, and large detecting units 94B, of collection angles  $\delta 5$ , at the periphery. It will be appreciated that other arrangements  
25 of detecting units of different sizes may be used.

It will be appreciated that a combination of these may be used. For example, the block 90 may include wide-angle collimators (Figure 17C) at the periphery and normal collimators of 90-degrees (Figure 17A) at the center.

It will be appreciated that the camera 10 may contain blocks 90 and (or)  
30 detecting units 12 of different collection angles.

Referring further to the drawings, Figures 17I and 17J schematically illustrate a detecting unit 12A with an adjustable collimator 96Z, for adjusting the collection angle, in accordance with embodiments of the present invention. Preferably, the

detecting unit 12A includes the detector 91 and an adjustor 91A at the bottom of the collimator 96Z. Additionally, the collimator 96Z is formed of a plurality of petal collimators 96A, 96B, 96C, and so on, wherein the collimator 96Z may be partially open, as shown in Figure 17I, or fully open, as shown in Figure 17J, by the action of the adjustor 91A, which may be, for example, a rotating knob, controlled by the data-processing system 126 (Figures 2, 3A). Preferably, the extent of opening of the collimator 96Z is adjustable, so it may be essentially closed, with the petal collimators 96A, 96B, 96C and so on substantially vertical with the detector 91, partially open, or fully open, much like a flower.

Figures 17K – 17N schematically illustrate the block 90, wherein the detector 91 is a single-pixel scintillation detector, such as NaI(Tl), LSO, GSO, CsI, CaF, or the like, operative with photomultipliers 103.

As seen in Figure 17K, the block 90, having proximal and distal ends 109 and 111, respectively, vis a vis an operator (not shown), is formed of the scintillation detector 91, of a single pixel, and the collimators 96, to create the detecting units 12. A plurality of photomultipliers 103 is associated with the single pixel scintillation detector 91, and with dedicated algorithms, as known, their output can provide a two dimensional image of the scintillations in the single pixel scintillation detector 91. In essence, this is an Anger camera, as known.

The distal view 111 of the collimator grid is seen in Figure 17L.

Two optional proximal views 109 of the photomultipliers 103 are seen in Figures 17M and 17N, as a square grid arrangement, and as an arrangement of tubes.

The detector may be a room temperature, solid-state CdZnTe (CZT) detector, configured as a single-pixel or a multi-pixel detector, obtained, for example, from eV Products, a division of II-VI Corporation, Saxonburg Pa., 16056, or from IMARAD IMAGING SYSTEMS LTD., of Rehovot, ISRAEL, 76124, [www.imarad.com](http://www.imarad.com), or from another source. A detector thickness  $\tau_d$  may range from about 0.5 mm to about 100 mm, depending on the energy of the radioactive emission and typically about 2 mm to about 50 mm, and in some cases about 5 mm to about 30 mm.

Alternatively, another solid-state detector such as CdTe, HgI, Si, Ge, or the like, or a scintillation detector (such as NaI(Tl), LSO, GSO, CsI, CaF, or the like, or a combination of a scintillation detector and a photomultiplier, to form an Anger

camera, or another detector as known, may be used. Additionally, a combination of scintillation materials and photodiode arrays may be used.

It will be appreciated that the methods of the present invention apply to pathological features that may be modeled as regions of concentrated radiations, or hot regions, regions of low-level radiation, which is nonetheless above background level, and regions of little radiation, or cold regions, below the background level. However, in general, for identifying a pathological feature of the heart, they relate to cold regions.

It will be appreciated that the methods of the present inventions may be operable by computer systems and stored as computer programs on computer-readable storage media.

It will be appreciated that the body may be an animal body or a human body.

It will be appreciated that the radioactive-emission-camera systems, cameras and methods of the present invention may be used with commonly owned US Applications 20040015075 and 20040054248 and commonly owned PCT publication WO2004/042546, all of whose disclosures are incorporated herein by reference. These describe systems and methods for scanning a radioactive-emission source with a radioactive-emission camera of a wide-aperture collimator, and at the same time, monitoring the position of the radioactive-emission camera, at very fine time intervals, to obtain the equivalence of fine-aperture collimation. In consequence, high-efficiency, high-resolution, images of a radioactive-emission source are obtained.

Commonly owned US application 20040054248 and commonly owned PCT publication WO2004/042546 further disclose various extracorporeal and intracorporeal systems, of radioactive-emission cameras, of relatively wide apertures, associated with position-tracking devices.

It will be appreciated that the radioactive-emission-camera systems, cameras and methods of the present invention may be used with commonly owned US Patent 6,173,201 to Front, whose disclosure is incorporated herein by reference, as well as by M. W. Vannier and D. E. Gayou, "Automated registration of multimodality images", Radiology, vol. 169 pp. 860-861 (1988); J. A. Correia, "Registration of nuclear medicine images, J. Nucl. Med., vol. 31 pp. 1227-1229 (1990); J-C Liehn, A. Loboguerrero, C. Perault and L. Demange, "Superposition of computed tomography and single photon emission tomography immunoscintigraphic images in the pelvis:

validation in patients with colorectal or ovarian carcinoma recurrence", Eur. J. Nucl. Med., vol. 19 pp. 186-194 (1992); F. Thomas et al., "Description of a prototype emission transmission computed tomography imaging system", J. Nucl. Med., vol. 33 pp. 1881-1887 (1992); D. A. Weber and M. Ivanovic, "Correlative image registration", Sem. Nucl. Med., vol. 24 pp. 311-323 (1994); and Hasegawa et al., U.S. Pat. No. 5,376,795.

These relate to the acquisition of both a functional image of the body, such as a radioactive-emission image, and a structural image, such as an ultrasound, an x-ray, or an MRI image, and their co-registration on a single frame of reference.

10 In essence, several images may be acquired and co-registered to the same frame of reference, as follows:

i. a first functional image scan, based for example, on anti-CEA monoclonal antibody fragment, labeled by iodine isotopes, may be acquired for targeting CEA - produced and shed by colorectal carcinoma cells for detecting a pathological feature, such as colorectal carcinoma;

15 ii. a second functional image, based for example, on nonspecific-polyclonal immunoglobulin G (IgG), which may be labeled with  $Tc^{99m}$ , may be acquired for locating blood vessels and vital structures, such as the heart, or the stomach, co-registered with the first functional image and the pathological feature detected on it, in order to locate the pathological feature in reference to blood vessels and vital organs; and

20 iii. a structural image, such as an ultrasound image, may be used for general structural anatomy, co-registered with the first and second functional images, in order to locate the pathological feature in reference to bones and the general anatomic structure.

25 Thus, a physician may locate the pathological feature in reference to the blood vessels, vital organs, and the bones, and guide a minimally invasive surgical instrument to the pathological feature, while avoiding the blood vessels, vital organs, and bones. The minimally invasive surgical instrument may be a biopsy needle, a wire, for hot resection, a knife for cold resection, an instrument of focused energy, to produce ablation, for example, by ultrasound, or by laser, an instrument for cryosurgery, an instrument for cryotherapy, or an instrument for brachytherapy,



wherein seeds of a radioactive metal are planted close to a tumor, for operating as a radioactive source near the tumor.

Commonly owned PCT publication WO2004/042546 further discloses that the surgical instrument may be visible on at least one of the images, for example, on the structural image, to enable the physician to see the instrument, the pathological feature, and the surrounding anatomy on the display 129 (Figure 3A). Additionally, the surgical instrument may be radioactively labeled, to be visible also on the functional image. PCT publication WO2004/042546 further disclose various extracorporeal and intracorporeal systems, of radioactive-emission cameras, and structural imagers such as an ultrasound camera or an MRI camera.

Commonly owned US Patent 6,173,201, to Front further discloses a method of stereotactic therapy, wherein a frame, which includes at least three markers, visible on a structural image, is rigidly secured to a patient. The structural image of a region inside the patient's body, which includes a pathological feature and the markers, is acquired. A functional image of the pathological feature is then acquired and co-registered with the structural image, to correlate the images to the same frame of reference. A stereotactic guide is rigidly attached to the frame and is used to guide a surgical instrument, such as a biopsy needle or a brachytherapy needle, to the pathological feature, with reference to the co-registered images.

Thus the radioactive-emission-camera systems, cameras and methods of the present invention may be used together with position tracking devices, for enhanced image acquisition, they may be used together with structural imager and structural imaging for correlating functional and structural images, and they may be used for guiding minimally invasive surgical instruments, such as a biopsy needle, a wire, for hot resection, a knife for cold resection, an instrument of focused energy, to produce ablation, for example, by ultrasound, or by laser, an instrument for cryosurgery, an instrument for cryotherapy, or an instrument for brachytherapy.

It will be appreciated that a structural image, such as by ultrasound may further be used and in order to provide information about the size and location of the body structure 215 for the purpose of creating the model 250 (Figure 5A).

It will be appreciated that a structural image, such as by ultrasound may further be used and in order to provide information about tissue attenuation, for example, as taught in conjunction by commonly owned PCT publication

WO2004/042546, whose disclosure is incorporated herein by reference. The information may then be used to correct the radioactive-emission measurements.

### **Active Vision**

5           At present, radioactive-emission imaging of a body structure is a three-stage process. First the radiopharmaceutical is administered. Then measurements are taken at a set of predetermined views, that is at predetermined locations, orientations, and durations. Finally, the data is analyzed to reconstruct the emission distribution of the volume and an image of the body structure is formed. The imaging process is  
10 sequential, and there is no assessment of the quality of the reconstructed image until after the measurement process is completed. Where a poor quality image is obtained, the measurements must be repeated, resulting in inconvenience to the patient and inefficiency in the imaging process.

          According to this embodiment, the present invention teaches using  
15 radioactive-emission measurements to define views for further radioactive-emission measurements of a body structure, to be performed during the current measurement process. Specifically, the methods teach analyzing the previously obtained measurement results to determine which further views are expected to provide a high quality of information. The analysis may be based directly on the photon counts  
20 obtained for the current or recent measurements and/or on a reconstruction of the body structure performed upon the completion of a set of measurements.

          The present embodiments address the problem of ensuring that the quality of data gathered during the measurement process is adequate to provide a high quality image. The collected data and/or the image reconstructed from the collected data is  
25 analyzed the while the measurement process is taking place. Based on the analysis, further views are defined. Since each view is associated with known values of the viewing parameter(s), selecting a view effectively specifies known viewing parameter values. The defined further views thus define a set of viewing parameter values, which are used during the current measurement process in order to collect data which  
30 yields a high-quality reconstruction of the body structure.

          The following embodiments are of a method for determining further views for the imaging of a body structure, and are not confined to a specific reconstruction

algorithm. Further views are preferably defined based on one or more of the following:

- 1) Detector photon count
- 2) Geometric properties of the reconstructed body structure
- 3) Information theoretic measures that quantify the quality of the data fed to the reconstruction algorithm

Each of these criteria is discussed in detail below.

Reference is now made to Figure 81 which is a self explanatory description of advantageous and disadvantageous viewing positions according to embodiments of the present invention.

Reference is now made to Figure 82, which is a simplified flowchart of a method of performing radioactive-emission measurements of a body structure, according to a preferred embodiment of the present invention. In step 200, radioactive-emission measurements of the body structure are performed at predetermined views, preferably in vivo. Preferably the measurements are performed for diagnostic purposes. These predetermined views are selected prior to the measurement process, based on a model of the body structure being imaged. In the model more and less informative viewing directions have been identified. The predetermined views of step 200 preferably include those views expected to be informative, based on an analysis of the model.

Preferably the body structure is all or a portion of: a prostate, a heart, a brain, a breast, a uterus, an ovary, a liver, a kidney, a stomach, a colon, a small intestine, an oral cavity, a throat, a gland, a lymph node, the skin, another body organ, a limb, a bone, another part of the body, and a whole body.

In step 210 the radioactive-emission measurements are analyzed. Preferably the analysis includes one or more of:

- 1) Analyzing detector photon count(s)
- 2) Analyzing detector photon count rate(s) and rate changes from one view to another
- 3) Identifying detector saturation
- 4) Reconstructing a body structure image from emission measurements
- 5) Identifying geometric properties of the reconstructed image
- 6) Applying information-theoretic measures to the reconstructed image

In step 220, further views for measurements are dynamically defined, based on the analysis performed in step 210. Preferably, each of the views is associated with viewing parameters selected from the group consisting of: detector unit location, detector unit orientation, collection angle, and measurement duration. Defining a  
5 view consists of providing a value for each of the parameters associated with the given view. The analysis (step 210) and/or dynamic view definition (step 220) may take into account external parameters including: measurement duration, time elapsed from the administration of the pharmaceutical to the measurement, radiopharmaceutical half life, radioactive emission type, and radioactive emission  
10 energy.

Each of these analysis techniques, and their application to view definition, is now discussed in turn. While each of the analysis/view determination techniques is discussed as a separate embodiment, multiple techniques may be used together to obtain the desired image quality.

15 In a first preferred embodiment, a photon count analysis ensures that the photon count at a given view yields an acceptable measurement error. As discussed above, the radiative emissions of the body structure being imaged is a Poisson process. In a Poisson process the Poisson noise grows inversely to the square root of the number of photons detected. In other words, if N photons are collected from a  
20 given view, the resulting signal to noise ratio (SNR) equals:

$$SNR = \frac{N}{\sqrt{N}} = \sqrt{N} \quad (12)$$

The unprocessed detector photon count at a given view thus provides significant information regarding the quality of the information obtained at a given view. If the photon count is too low, it may be desired to continue to collect photons  
25 at the current location/orientation in order to obtain a satisfactory SNR. Alternatively, it may be determined that enough photons have already been collected, and to terminate the current view and move on to the next view.

The analysis is preferably performed by defining a global or local required measurement error, and comparing the square root of the obtained photon count to the  
30 required measurement error. Photon count analysis can be applied to the current and/or previous views. When a photon count of a current view is found to be too low, the duration of the current view is preferably extended in order to obtain the required

error value. When a photon count of a past view is found to be too low, an emission measurement at substantially the same location and orientation but having a longer duration than previously is preferably performed. Alternately or additionally, the collection angle at the given location/orientation is preferably increased.

5 In an additional preferred embodiment, a detector photon count is analyzed to identify detector saturation at a given view. Preferably, when a detector is determined to have saturated, a new view or views are selected to reinforce those views that have saturated. In an alternate preferred embodiment, further views are defined to avoid highly-radiating portions of the body structure.

10 In a second preferred embodiment, a photon collection rate at a given view is analyzed to determine if it is within a specified range. In the preferred embodiment, the photon count rate is used to identify regions of high or low interest. In prostate imaging, for example, a region of high interest may be identified by a high photon rate, indicative of a tumor. In a second example, a region of high interest may be  
15 identified in heart imaging by a low photon rate, indicative of non-functional tissues. After one or more areas of high and/or low interest are found, further views are preferably defined by selecting views to concentrate on regions of high interest and/or to avoid regions of low interest. It is thus possible to zoom in on a suspected pathology without repeating the emission measurement process.

20 In a further preferred embodiment, the analyzing of step 210 includes reconstructing a radioactive-emission density distribution of the body structure. Reconstruction may be performed according to any applicable technique known in the art. The reconstruction is then used as the basis for further analysis.

Reconstruction based on the data collected from the predetermined views  
25 provides information regarding the quality of information obtained from the preceding measurements, and which further views are likely to be most informative. Selecting new views based on reconstruction is intended to bring us into viewing from the more informative views or combinations of views.

Reference is now made to FIGURES 83 and 84a-84b, which pictorially  
30 illustrate how different views provide differing types and quality of information. Figure 3 shows an object 300 shaped as a cylinder with a front protrusion, and having a high-emittance portion (hotspot) 310. Four views of object 300 are shown, which can be seen to provide different levels of information. Front views, such as  $V_1$ ,

provide little information regarding the shape of object 300 and have relatively little attenuation between the detector and hotspot 310. Side views, such as  $V_2$ , provide edge information regarding the object shape or profile, and when correlated with front views help locate hotspot 310 spatially within object 300. Top views, such as  $V_3$ , provide information regarding the cylinder edge region 320. Finally, rear views, such as  $V_4$ , are uninformative about the shape of object 300 and have high attenuation relative to hot region 310.

FIGURES 84a and 84b demonstrate how the proper selection of views may improve the quality of information obtained for the body structure, for example in distinguishing between two regions of interest within a given volume.

Figure 84a illustrates an object 400 having two high-emission regions of interest (ROI), 410 and 420. For clarity the views  $V_A$  to  $V_F$  are shown as lines in Figure 84a, however in practice they will each have a finite collection angle  $\delta$ . The position of ROIs 410 and 420 are assumed to have been estimated based on a model of object 400 and/or a previously performed prescan. A goal of an aspect of the present invention is to select an additional new view or views which increase the information we have regarding the separation of ROIs 410 and 420 within object 400.

In simple terms, consider the object as having three regions: ROI 410 with intensity  $I_1$ , ROI 420 with intensity  $I_2$ , and a low-emission region 430 between the two ROIs with intensity  $I_3$ . The detected intensity at a given detector is proportional to  $\frac{I_n}{r_{ni}^2}$ , where  $I_n$  is the emission intensity of region  $n$  and  $r_i$  is the distance of region  $n$  from detector  $V_i$ .

Figure 84b illustrates the added information provided by each of the shown views,  $V_A$  to  $V_F$ . Views  $V_B$  and  $V_C$  collect emissions from all three regions, and are therefore least informative. Views  $V_D$  and  $V_E$  collect emissions from only low emittance region 430, and therefore provide most information regarding the location of each ROI within the volume and the separation between ROIs 410 and 420. Views  $V_A$  and  $V_F$  pass only through a single ROI, and therefore provide an intermediate level of information. It is a goal of the present invention to determine, while the emission measurements of the body structure are taking place, that views in the vicinity of  $V_D$  and  $V_E$  are highly informative, and to add these further views to the measurement process.



A body structure reconstruction can be utilized in several ways to define further views. A first way is to identify interesting portions of the contour and structure of the reconstruction. For example, it is seen in Figure 83 that top views are informative about edge region 320. Further top view measurements will therefore be  
5 informative re edge region 320, and may enable defining the edge more accurately.

In a preferred embodiment, the reconstruction is analyzed to identify textural edges within the reconstruction, and view definition preferably includes selecting views at an angle to the textural edges. In the preferred embodiment, the angle is a substantially sharp angle in order to provide information regarding the edge.

10 In another preferred embodiment, the reconstruction is analyzed to identify volumetric boundaries within the reconstruction, and view definition preferably includes selecting views at an angle to the volumetric boundaries. It is expected that the defined views will provide information regarding the boundary and differences in surrounding tissues on either side of the boundary. In the preferred embodiment, the  
15 angle is a substantially sharp angle.

Another way to utilize the reconstruction to define further views is to identify suspected organ targets within the reconstruction, and to select further view(s) in close proximity to the suspected organ targets. A suspected organ target is typically detected by identifying portions of the reconstruction whose emission intensity  
20 distribution and spatial characteristics are typical of a suspect region.

In a first preferred embodiment, a suspected organ target is defined as a high-emittance portion of the reconstruction. In a second preferred embodiment, a suspected organ target is defined as a low-emittance portion of the reconstruction.

In the preferred embodiment the further views are used immediately for  
25 radioactive-emission measurements. The results of the new measurements are then used in another analysis to define new further views for additional measurements. The radioactive-emission measurements may then be said to be performed iteratively.

Reference is now made to Figure 85a, which is a simplified flowchart of an iterative method of performing radioactive-emission measurements of a body  
30 structure, according to a first preferred embodiment of the present invention. In step 500, radioactive-emission measurements of the body structure are performed at predetermined views. In step 510, an analysis is performed of the previously performed emission measurements. In step 520 a decision is made whether to

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continue with further measurements. If yes, in step 530 further views are defined based on the analysis. Subsequent iterations continue until the decision to end the emission measurement process. After the first iteration, the analysis performed at a given stage may include consideration of all or on part of the measurements performed during one or more previous iterations, in addition to the new measurements.

Reference is now made to Figure 85b, which is a simplified flowchart of a iterative method of performing radioactive-emission measurements of a body structure, according to a second preferred embodiment of the present invention. In the present preferred embodiment, a reconstruction of the body structure is formed in step 505. The analysis step 510 is then performed utilizing data provided by the reconstruction(s).

Referring again to Figure 82, preferably, analysis step 210 includes determining an accuracy of the reconstruction. Accuracy is preferably determined by analyzing the variance of the reconstructions formed over multiple iterations. Preferably, further views are defined in step 220 to concentrate on the region for which higher accuracy is required. Regions of the reconstruction having low variance provide a high degree of confidence regarding the accuracy of the reconstruction in the given region (where a portion may include the entirety of the body structure being imaged). Further views may be added to the current measurements until the variance is reduced to a required level.

Preferably, analysis step 210 includes determining a resolution of the reconstruction. Resolution is preferably determined by analyzing the full width at half maximum (FWHM) of peak values of the reconstruction. The FWHM is given by the distance between points at which the reconstructions reaches half of a peak value. Preferably, further views are defined in step 220 to concentrate on the region for which higher resolution is required.

An additional way to define future views using the reconstruction is on an information-theoretic basis. A quality function expressing an information theoretic measure is defined. The quality function rates the information that is obtainable from the body structure when one or more permissible views are added to current measurement process. Several examples of quality functions based on information-theoretic measures are discussed in detail below. The quality function is used to rate

potential further views. The measurement process may then continue at those further views whose addition to the previous views yields a high rating.

Reference is now made to Figure 86a, which is a simplified flowchart of a method for dynamically defining further views, according to a first preferred embodiment of the present invention. In step 610 a quality function is provided. The quality function expresses an information-theoretic measure which rates the quality of information obtainable from potential further views. In step 620 a set of further views is selected to maximize the quality function. Preferably the selected further views fulfill certain constraints; for example the further views may be selected from a predefined set or may be located in the vicinity of a region of interest within the body structure.

In the above described reconstruction-based analyses, the quality function is evaluated independently for a single reconstruction of the emission intensity of the body structure. However, quality functions may be defined which calculate the score for a given set in relation to one or more reconstructions and/or emittance models. As is further discussed herein, given an object or class of objects, emittance models may be devised to reflect expected or typical emission patterns for the given object.

For simplicity, the following discussion describes the evaluation of information-theoretic quality functions based on emittance models only. It is to be understood that at least one of the emittance models is a reconstruction of the body structure based on past measurements. Any remaining emittance models are provided externally, and may be based on general medical knowledge or on information gathered during a previous round of emission measurements of the body structure.

Reference is now made to Figure 86b, which is a simplified flowchart of a method for dynamically defining further views, according to a second preferred embodiment of the present invention. The current method differs from the method of Figure 86a by the addition of steps 605-606. In step 605 a set of one or more emittance models is provided (where the set includes one or more reconstructions of the body structure). An emittance model specifies the radiative intensity of each voxel in the body structure. As discussed above, some of the viewing parameters affect the radiative intensity of the voxels in the volume, for example the type of radiopharmaceutical and the time since administration of the radiopharmaceutical. Therefore, the emittance models provided in step 605 preferably correspond to the

relevant viewing parameters. In step 606 a collection of possible further views of the body structure is provided. The collection of views includes possible further views for future measurements, preferably based on anatomical and other constraints. Furthermore, the quality function provided in step 610 may utilize multiple emission  
5 models.

In the preferred embodiment, one or more of the emittance models contains at least one high-emittance portion (i.e. hot region). A prostate containing a tumor, for example, may be modeled as an ellipsoid volume with one or more high-emittance portions.

10 In the preferred embodiment, one or more of the emittance models contains at least one low-emittance portion. A diseased heart may therefore be modeled as a heart-shaped volume with low-emittance portions.

Note that an emittance model need not contain high- or low- emittance portions, but may have a uniform intensity or a slowly varying intensity.

15 In a first preferred embodiment the quality function implements a separability criterion. The implementation and evaluation of the separability criterion for active view determination is performed substantially as is further described herein..

In a second preferred embodiment, the quality function implements a  
20 reliability criterion. The implementation and evaluation of the reliability criterion for active view determination is performed substantially as described herein.

Maximization of the quality function may be performed utilizing any method known in the art such as simulated annealing and gradient ascent. In the simulated annealing (SA) method, each point of the search space is compared to a state of some  
25 physical system. The quality function to be maximized is interpreted as the internal energy of the system in that state. Therefore the goal is to bring the system from an arbitrary initial state to a state with the minimum possible energy.

The neighbors of each state and the probabilities of making a transition from each step to its neighboring states are specified. At each step, the SA heuristic  
30 probabilistically decides between moving the system to a neighboring state  $s'$  or staying put in states. The probabilities are chosen so that the system ultimately tends to move to states of lower energy. Typically this step is repeated until the system reaches and acceptable energy level.

Gradient ascent, on the other hand, is based on the observation that if a real-valued function  $F(x)$ , such as the quality function of the present embodiments, is defined and differentiable in a neighborhood of a point  $a$ , then  $F(x)$  increases fastest if one goes from  $a$  in the direction of the gradient of  $F$  at  $a$ ,  $\nabla F(a)$ . It follows that if:

$$5 \quad b = a + \gamma \nabla F(a) \quad (19)$$

for  $\gamma > 0$  a small enough number, then  $F(a) \leq F(b)$ . Gradient ascent starts with a guess  $x_0$  for a local maximum of  $F$ , and considers the sequence  $x_0, x_1, x_2, \dots$  such that:

$$x_{n+1} = x_n + \gamma \nabla F(x_n), \quad n \geq 0. \quad (20)$$

10 Since  $F(x_0) \leq F(x_1) \leq F(x_2) \leq \dots$ , the sequence  $(x_n)$  is expected converges to a local maximum.

Preferably, the set of views selected with the quality function is increased by at least one randomly selected view. The randomly selected view(s) increase the probability that the quality of information obtained with the further views is  
15 maximized globally rather than locally.

As discussed above, selecting the best set of size  $N$  from amongst a large set of candidate projections is computationally complex. Since the size of the collection of views and of the required set may be large, a brute force scheme might not be computationally feasible.

20 In an additional preferred embodiment, a so-called "greedy algorithm" is used to incrementally construct larger and larger sets, until the required number of further views is defined. When multiple further views are required, it is computationally complex to maximize the quality function over all possible combinations of further views. The greedy algorithm reduces the computational burden by selecting the  
25 further views one at a time. The algorithm starts with a current set of views, and for each iteration determines a single view that yields the maximum improvement of the set score (hence the name "greedy").

In theoretical terms, assume  $\rho(\cdot)$  is the quality measure we are using for the view selection, and assume without loss of generality that we are trying to maximize  
30 this measure. We gradually build a set  $W$  of projections as follows. We start with an empty set  $W = \emptyset$ , and at every stage choose the projection that maximizes the quality measure when added to the current set:



$$W \leftarrow \arg \max_{W'} \{ \rho(W') \mid W' = W \cup \{ \phi \}, \phi \in \Phi \} \quad (21)$$

In other words, during a given iteration, a respective score is calculated for a combination of the previous set with each of the views which is not a member of the current set. The current set is then expanded by adding the view which yielded the highest respective score, and the expanded current set serves as the input to the following iteration. Thus the number of times the scoring function is calculated per iteration drops from iteration to iteration. For a large collection of possible views, the greedy algorithm reduces the total number of computations required for set selection.

Reference is now made to Figure 87, which is a simplified flowchart of an iterative “greedy” method for defining further views, according to a preferred embodiment of the present invention. The greedy algorithm is implemented substantially as described herein. In step 1000 a collection of views of the body structure is provided. The collection of views includes possible further views for future measurements, preferably based on anatomical and other constraints. In step 1010, the set of views used for the previous emission measurements is established as a current set of views. In step 1020 the view set is incrementally increased by a single further view during each iteration, until the required number of further views has been selected.

Reference is now made to Figure 88, which is a simplified flowchart of a single iteration of the view selection method of Figure 87, according to a preferred embodiment of the present invention. The method of Figure 88 expands the current set of views by a single view. The method begins with a current set of views, which is the predetermined set (step 1010 above) for the first iteration of the greedy algorithm, or the set formed at the end of the previous iteration (step 1120 below) for all subsequent iterations. In step 1100, a respective expanded set is formed for each view not yet in the current set of views. A given view’s expanded set contains all the views of the current set of views as well as the given view. In step 1110, a respective score is calculated for each of the expanded sets using the quality function. In step 1120, the view which yielded the highest-scoring expanded set is selected as a further view, to be used for further radioactive emission measurements. Finally, in step 1130, the current set is equated to the highest-scoring expanded set by adding the selected



view to the current set. The newly formed current set serves as an input to the subsequent iteration, until the desired number of views is attained.

Reference is now made to Figure 89, which is a simplified flowchart of a method for dynamically defining further views, according to a third preferred embodiment of the present invention. In step 1210, a collection of possible further views for performing radioactive-emission measurements of the body structure are provided. Each of the views is associated with at least one viewing parameter. Preferably the viewing parameters consist of at least one the following: detector unit location, detector unit orientation, collection angle, and measurement duration.

In step 1220 at least one quality function is provided. Each quality function is for evaluating sets of views, essentially as described above. A single quality function may be used to select several sets of views, where each set of views contains a different number of views.

In step 1230, multiple sets of further views (where a set may include a single further view) are formed from the collection of views, using the quality function(s) provided in step 1220. In a first preferred embodiment, each of the sets is formed using a different one of the quality functions. In an alternate preferred embodiment, one or more of the quality functions are used to form more than one set of views, where sets formed with the same quality function have differing numbers of views.

In step 1240, a selected set of views is obtained from the sets formed in step 1230.

In a first preferred embodiment, the final set of views is obtained by choosing one of the sets formed in step 1230 using a set selection criterion. For example, a respective set is formed in step 1230 for the separability and reliability criteria independently. A set selection criterion which calculates an overall performance rating for a given set taking both criteria into account is defined, and the formed set with the highest overall rating is selected as the final set.

In another preferred embodiment, the selected set of views is obtained by merging the sets formed in step 1230 according to the relative importance of the respective quality function used to form each set.

In the preferred embodiment, the method further consists of providing at least one emittance model and/or reconstruction representing the radioactive-emission

density distribution of the volume, and of evaluating with at least one of the quality functions of step 1220 is performed in relation to the emittance models.

As discussed above, since each view is associated with one or more parameters, the selected set yields a group of parameter values for performing  
5 effective detection of the intensity distribution of the body structure. For example, if each view is associated with a view location parameter the selected set defines a set of locations for collecting emission data from an object, in order to provide a high-quality reconstruction of the intensity distribution of the body structure.

Reference is now made to Figure 90, which is a simplified block diagram of  
10 measurement unit for performing radioactive-emission measurements of a body structure, according to a preferred embodiment of the present invention. Measurement unit 1300 includes probe 1310, analyzer 1320 and view definer 1330. Probe 1310 performs the radioactive-emission measurements of the body structure. Radioactive-emission-measuring probe 1310 preferably comprises several detecting  
15 units, which may be of different geometries and different collection angles  $\delta$ , within a housing. Preferably, the orientation and/or collection angle of the individual collimators is controllable. Analyzer 1320 analyzes the radioactive-emission measurements obtained from probe 1310. View definer 1330 dynamically defines further views for measurements, based on the analysis provided by analysis unit 1320.  
20 The analysis and view definition are performed substantially as described above.

The abovedescribed methods for radioactive-emission measurements of a body structure begin by performing measurements at a predetermined set of views. The results of the initial measurements are then analyzed and further views are defined.

The initial set of views is preferably selected based on information theoretic  
25 measures that quantify the quality of the data fed to the reconstruction algorithm, in order to obtain the best data for reconstructing a three-dimensional image of the body structure, as described herein. The following section concentrates on the second step of the process, namely, obtaining the optimal and permissible set of initial views for performing the radioactive-emission measurements of the body structure. The initial  
30 predetermined set of views is denoted herein the optimal set of views.

The initial predetermined set of views is preferably selected in accordance with the method of the view selection as described herein. Preferably the initial

predetermined set of views is selected on the basis of one or a combination of the separability, reliability, and uniformity criteria.

The abovedescribed methods may each be embodied as a computer program stored on a computer-readable storage medium. In the preferred embodiment, computer-readable storage medium contains a set of instructions for defining views for radioactive-emission measurements of the body structure. An analysis routine analyzes the radioactive-emission measurements obtained from a radioactive-emission-measuring probe, and a view definition routine dynamically defines further views for measurements, based on the analyzing.

By enabling high-quality reconstruction based on data collected from a limited collection of views, the abovedescribed view set selection techniques present a way to resolve the current conflict between the relatively large-pixel detectors needed for measurement speed and data processing considerations, with the small-pixel detectors needed until now to obtain a high-resolution reconstruction. The data obtained using the selected set of views enables a high-resolution reconstruction from a smaller number of measurements. Additionally, reconstructing the intensity distribution from a smaller quantity of collected data simplifies the computational process. The abovedescribed embodiments are particularly suitable for medical imaging purposes, where a high-resolution image is needed and it is desired to minimize the difficulties of the patient undergoing the diagnostic testing or treatment.

### **Voxel Dynamic Modeling**

Dynamic modeling is a technique in which the parameters of a dynamic system are represented in mathematical language. Dynamic systems are generally represented with difference equations or differential equations. Measurements obtained from the modeled system can then be used to evaluate the values of parameters of interest that cannot be measured directly.

In the present case, the system being modeled is the body structure (or portion thereof) being imaged. During imaging, the emittance from a given voxel is affected by the chemical properties of the radiopharmaceuticals well as by the half-life of the tracer, as well as by the nature of the body structure being imaged. For example, the chemical properties of the antibody to which the tracer is attached govern factors such as binding to the tissue, accumulation, and clearance rate.

The goal of the presented models is to recover the kinetics per voxel of one or more parameters of interest. Each of the models reflects a different mechanism for the diffusion of the radiopharmaceutical into and out of the voxel, as well as the possibility of accumulation within the voxel. For a given measurement process the dynamic model should be selected to match the known properties of the radiopharmaceutical being used.

Reference is now made to Figure 91, which is a simplified flowchart of a method for measuring kinetic parameters of a radiopharmaceutical in a body, according to a preferred embodiment of the present invention. In step 6010, the radiopharmaceutical is administered to the body. In step 6020, the body or a portion of the body are imaged. In step 6030, a model is provided for obtaining kinetic parameters from the imaging is provided. Several preferred embodiments of dynamic models are presented below. Finally, in step 6040, the kinetic parameters are obtained by applying the measurements to the provided model in order to extract the value of the required parameter(s). The kinetic parameters may provide information on factors such as actual uptake, rate of uptake, accumulation, and clearance of the radiopharmaceutical, which in turn provide information about the health of tissue in the voxel. The obtained parameter values can thus be analyzed to evaluate the health of the imaged body structure and of other portions of the body (for example renal functioning). (See description of expert system) The parameter values can also be analyzed and used to control future administration of the radiopharmaceutical (See description of closed loop injection system). The parameters obtained in step 6040 preferably include at least one of: local (in-voxel) representation of blood pool, blood flow, and diffusion to and/or from the local tissue *as representative of function (e.g. viability)*.

Three preferred embodiments of dynamic models for provision in step 6030 are now presented. The following rationale and assumptions are common to all of the presented embodiments.

The analysis is of one voxel versus the rest of the body, not of the entire organ.

The dynamic model relates the per pixel emission levels to factors such as the blood in voxel, the tissue in voxel (and uptake from blood), and blood re-fill (perfusion/flow).

An additional assumption is that the amount of the tracer in the voxel is insignificant compared with the rest of the body and with the global blood pool. Therefore, the voxel in the region of interest (ROI) is affected by the global blood pool, but does not affect it. As a result, the concentration of tracer in the global blood pool can be recovered separately by one or more of: modeling the known kinetics given the exact injected dose, measuring the concentration at a pre-identified blood region using the imaging equipment, or by taking blood samples over time.

It is also assumed that the concentration of the tracer in the global blood may be controlled in a complex fashion by various injection profiles, such as:

1) Bolus injection

2) Constant drip

3) Smart injection – in which the radiopharmaceutical is injected in a controlled manner over time. The smart injection profile may be predetermined, or responsive to external events and/or feedback from the imaging equipment (see closed loop description). For example, rather than injecting a single bolus dose of radiopharmaceutical, one can inject a tenth of the dose for each of a series of ten injections. Examples of smart injection profiles are described below.

It is assumed that in ischemic conditions, not enough blood flow reaches the voxel, thus the concentration of the tracer in the blood of that voxel is different than in global blood pool. For example, if oxygen is the tracer, then ischemic region has lower oxygen concentration in the capillaries than in global blood pool due to poor refill.

An additional assumption is that the processes affecting the tracer concentration are slower than fractions a second, so that the volume and flow values (as defined below) relate to an average over the heart cycle. Thus gating will not separate the uptake into the tissue for different time slices in the heartbeat. Gated analysis (which is synchronized with the heart cycle) may be developed for fast processes which do not involve slow accumulation in the muscle tissue, or, alternatively, model the accumulation, both of which requires motion compensation.

A final assumption is that each voxel is large enough so that variables may be defined to relate to the voxel structure in global terms. The dynamic models described below are for voxels having a millimetric size, which are therefore significantly larger than the blood vessels (unlike during imaging of blood

vessels). The models therefore include parameters for both blood and tissue parameters. In cases where a very high-resolution reconstruction (i.e. sub-millimetric) is required, a different model should be applied to handle voxels which are pure blood (e.g. voxels inside coronaries).

5 The following parameters are defined for all of the dynamic model embodiments presented below:

1)  $V_t$  - Volume of tissue in voxel.

2)  $V_b$  - Volume of blood within the capillaries in the given voxel.  $V_b$  is normally constant for a given tissue type, but may vary for different tissue types such  
10 as blood vessel, connective tissue, or tumor before or after angiogenesis

3)  $V$  - Voxel volume. The voxel volume is the sum of the tissue volume and blood volume within the voxel:

$$V = V_t + V_b \quad (1)$$

15

$V$  is a fixed value dictated by the imaging equipment (i.e. camera) performing the radioactive-emission measurements.

4)  $R_b$  - Density of blood within the voxel.  $R_b$  is the ratio of the volume of the blood in the voxel to the total voxel volume:

20

$$R_b = V_b / V \quad (2)$$

For example, in cross section, the diameter of a capillary is about 10-15 $\mu$ m. To allow diffusion to cells the capillaries are spaced about 50-150  $\mu$ m apart.  
25 Therefore, it is reasonable to assume that healthy tissue has  $R_b \sim 1-5\%$

5)  $F$  - Blood flow to voxel. It is assumed that blood flow is not affected by neighboring voxels (i.e. blood flow is of "fresh" blood from the arteries).

6)  $C_b$  - Tracer concentration in blood within the voxel (reflects the capillaries in the voxel).

30

7)  $C_t$  - Tracer concentration in tissue within the voxel.

8)  $C$  - Tracer concentration in voxel, as measured by the imaging equipment.

9)  $C_g$  - Tracer concentration in global blood. The concentration in the global blood supply is assumed to be given.  $C$  may be determined with a separate model, or



by measuring the global blood concentration directly. A full model of  $C_g$  should reflect many of the patient's conditions, including cardiac output, prior diseases (such as metabolic disorders or diabetes), hyper/hypo-fluid volume, hyper/hypo-blood pressure, liver and/or kidney function, drugs (diuretics), and so forth.

5       Note that all of the above parameters other than  $C_g$  are defined per voxel.

Reference is now made to Figure 92, which is a schematic representation of a dynamic model of a voxel, according to a first preferred embodiment of the present invention. The present embodiment (denoted herein model 1) assumes symmetric diffusion (i.e. the tracer diffusion coefficients into and out of the voxel are equal), and  
10       that there is no accumulation of the tracer within the voxel. Figure 92 illustrates the role of each of the parameters described above.

The radioactive pharmaceutical is introduced into the global blood pool 6110 by injection according to an injection profile 6120. The radiopharmaceutical is conveyed to the voxel via the circulatory system 6125. The radiopharmaceutical  
15       flows through the voxel via the capillaries 6130 running through the voxel at flow rate  $F$ . Diffusion from the capillaries 6130 to the voxel tissue 6140 (uptake) and from the voxel tissue 6140 to the capillaries 6130 (release) occurs with a common diffusion coefficient  $K_d$ .  $K_d$  is an effective coefficient which takes into account both the uptake and outtake diffusion coefficients, and the surface area to volume ratio of the  
20       capillaries 6130. The remainder of the pharmaceutical is dispersed to the rest of the body for uptake and clearance 6145.

Similar or identical components are indicated with the same reference numbers throughout the figures.

Model 1 assumes tracer delivery to the voxel by diffusion to and from the local  
25       tissue, rather than by accumulation and dissolution. Therefore, model 1 can serve for applications with materials like Thallium and CardioTech, but not with Mibi which accumulates due to different diffusion rates in and out of the tissue. Models 2 and 3, which are presented below, allow for accumulation, and are therefore more suitable for radiopharmaceuticals such as Mibi.

30       Equations 3-5 present the relationship between the kinetic parameters for model 1:

$$C = \frac{C_t \cdot V_t + C_b \cdot V_b}{V} \quad (3)$$

$$= C_b \cdot R_b + C_t \cdot (1 - R_b)$$

$$\frac{dC_t}{dt} = K_d(C_b - C_t) \quad (4)$$

$$\frac{dC_b}{dt} = \frac{F}{V_b}(C_g - C_b) - K_d(C_b - C_t) \quad (5)$$

5 Initial conditions:  $C_t = 0, C_b = 0$

C is measured dynamically by the imaging equipment and  $C_g$  is determined separately by measurement or independent modeling from the art.

10 Reference is now made to Figure 93, which is a schematic representation of a dynamic model of a voxel, according to a second preferred embodiment of the present invention. The present embodiment (denoted herein model 2) assumes symmetric diffusion, with a diffusion coefficient of  $K_d$ . As in model 1,  $K_d$  is an effective coefficient which takes into account both the uptake and outtake diffusion coefficients, and the surface area to volume ratio of the capillaries 6130. However, in  
15 contrast with model 1, model 2 assumes that a fraction 6150 of the tracer concentration within the tissue is accumulated and is not diffused back to blood (for example by metabolism). The tracer accumulation within the voxel occurs at a rate of A.

20 Equations 6-9 present the relationship between the kinetic parameters for model 2:

$$C = \frac{C_t \cdot V_t + C_b \cdot V_b}{V} + \text{Accum} \quad (6)$$

$$= C_b \cdot R_b + C_t \cdot (1 - R_b) + \text{Accum}$$

$$\frac{dC_t}{dt} = K_d(C_b - C_t) - A \cdot C_t \quad (7)$$

$$\frac{dC_b}{dt} = \frac{F}{V_b}(C_g - C_b) - K_d(C_b - C_t) \quad (8)$$

25  $\text{Accum} = \int_0^t A \cdot C_t \, dt \quad (9)$

Initial conditions:  $C_t = 0$ ,  $C_b = 0$ ,  $Accum = 0$

Reference is now made to Figure 94, which is a schematic representation of a dynamic model of a voxel, according to a third preferred embodiment of the present invention. The present embodiment (denoted herein model 3) assumes asymmetric diffusion, with uptake and release occurring according to the blood concentration (vs. zero) for uptake, and to the tissue concentration (vs. zero) for release, not according to the difference in concentrations (blood vs. tissue) as in model 1. Transport to the tissue is modeled by a diffusion coefficient of  $K_{in}$ , depending only on the outside concentration of capillary blood. Outgoing transport is modeled by a diffusion coefficient of  $K_{out}$  for outgoing transport, depending only on the internal (tissue) concentration. This way, accumulation is described by a high  $K_{in}$  and a low  $K_{out}$ .  $K_{in}$  and  $K_{out}$  are effective coefficients, which account for the surface area to volume ratio of capillaries.

Equations 10-12 present the relationship between the kinetic parameters for model 3:

$$C = \frac{C_t \cdot V_t + C_b \cdot V_b}{V} \quad (10)$$

$$= C_b \cdot R_b + C_t \cdot (1 - R_b)$$

$$\frac{dC_t}{dt} = K_{in} \cdot C_b - K_{out} \cdot C_t \quad (11)$$

$$\frac{dC_b}{dt} = \frac{F}{V_b} (C_g - C_b) - K_{in} \cdot C_b + K_{out} \cdot C_t \quad (12)$$

Initial conditions:  $C_t = 0$ ,  $C_b = 0$

Models 2 and 3 are suitable for use with tracers like Thallium and Mibi, since they do not assume symmetric diffusion to/from the local tissue, but rather allow accumulation.

Regarding the parameters of the abovedescribed dynamic models, it may be possible to attribute the physiological meaning as follows:

- 1)  $F$  may correspond to perfusion
- 2)  $K_d + A$  may correspond to viability and metabolism (Model 2)
- 3)  $K_{in}$  may correspond to viability (Model 3)

Referring again to Figure 92, in step 6040 the kinetic parameters for the voxel are obtained by applying the measured values to the provided model and extracting the value of the required parameters. Parameter extraction may be performed utilizing any technique known in the art, such as numerical analysis. Repeated measurements may be made of the given voxel, and the parameters calculated with increasing accuracy.

In a preferred embodiment, parameter extraction the dynamic system is provided in step 6030 as an analogous RLC electronic circuit. An RLC circuit is an electrical circuit consisting of resistors (R), inductors (L), and capacitors (C), connected in series and/or in parallel. Any voltage or current in an RLC circuit can be described by a second-order differential equation. Since all of the abovedescribed models present the voxel kinetic parameters as a second order system, the dynamic model provided in step 6030 may be described as an arrangement of resistors, capacitors, and inductors.

Voltage analysis of an RLC circuit is based on expressing the voltage over each of the circuit elements as a function of the circuit current as follows:

$$\text{Resistor: } V_R(t) = R \cdot i(t) \quad (13)$$

$$\text{Capacitor: } V_C(t) = \frac{1}{C} \int_{-\infty}^t i(\tau) d\tau \quad (14)$$

$$\text{Inductor: } V_L(t) = L \frac{di}{dt} \quad (15)$$

As an example of RLC circuit analysis, consider the series RLC circuit 6160 shown in Figure 95. RLC circuit 6160 consists of resistor 6165, inductor 6170, and capacitor 6175 connected in series, with an input voltage provided by voltage source 6180. In a series RLC circuit, the total voltage drop over the circuit is the sum of the voltage drop over each of the circuit elements, so that:

$$V(t) = R \cdot i(t) + L \frac{di}{dt} + \frac{1}{C} \int_{-\infty}^t i(\tau) d\tau \quad (16)$$

and:

$$\frac{dV}{dt} = L \frac{d^2I}{dt^2} + R \frac{di}{dt} + \frac{1}{C} i(t)$$

(17)

Presenting the dynamic model as an RLC circuit enables using well-known circuit analysis techniques to derive the values of the desired parameters based on the measurements, and to analyze the behavior of the dynamic system. In terms of the abovedescribed dynamic modeling, the voltage,  $V$ , represents the administered radiopharmaceutical, and  $dV/dt$  represents the rate of change of the administered radiopharmaceutical, that is the administration protocol. The circuit function (e.g. the right hand side of equation 17) is analogous to the obtained image. Since the obtained image is dependent on  $\emptyset$ , the probability that a photon emitted by the given voxel is detected by the imaging equipment, the circuit function is a function of  $\emptyset$ . The RLC analogy can thus be used in order to determine the radiopharmaceutical input function,  $dV/dt$ , which optimizes  $\emptyset$ .

Possible forms for  $dV/dt$  include bolus injection ( $V(t)$  is a single pulse at  $t=0$ ), constant drip ( $V(t)$  is a constant), and smart injection profile. Following are non-limiting examples of smart injection profiles:

- 1) Randomly (e.g. in the range of about every 1 to 200 sec)
- 2) Periodically every  $T$  seconds
- 3) Synchronized to the camera acquisition cycle. For example, if the camera produces a full volume scan every 5 seconds the injections are synchronized with each repetition of the scan. Synchronizing with camera acquisition allows better spatio-temporal coverage, as the injection and the scanning plans may be optimized together.
- 4) Synchronized to motion-related events. Motion-related events may include one or more of expiration, inspiration, cardiac movement, stomach contraction, gastro-intestinal movement, joint movement, organ movement, and so forth. For example, motion-synchronized injection may be used to inject and/or acquire during a relatively stable time period or a relatively motion-intensive time period.
- 5) Synchronized to physiological events (which may be acquired by another system). Physiological events may include a change in the activity of an organ or tissue (such as  $O_2/CO_2$  concentration), glucose concentration, changes in perfusion,

electrical activity (ECG, EMG, EEG, etc...), neuronal activity, muscular activity, gland activity, and so forth.

6) Synchronized to an external event, for example to an external stimulation (e.g. by motion, sound, or light) or drug administration. Synchronizing with a drug  
5 administration may be useful for procedures such as imaging of cerebral perfusion events (like in functional MRI), so that a small bolus may be injected per stimulus and the region that uptakes the radiopharmaceutical will be more likely to be related to the stimulus.

7) Responsive to the radiopharmaceutical concentration in the blood. By  
10 monitoring the level of the radiopharmaceutical in the blood (either by drawing blood samples or by determining the level with the camera or other measurement system) it is possible to control the pattern in the blood, for example to keep a desired level, a desired slope, cycles, and so forth. In particular, when the frequency domain is used for the final analysis it may be beneficial to have the injection profile in one or more  
15 fixed periods (frequencies) selected to fit the expected kinetic profile, and to keep the concentration in the blood controlled so as to produce a desired spectral performance of the blood concentration, for example an approximately sinusoidal, saw-tooth, other harmonic form. When the level in the blood is provided by the camera, a closed loop system is obtained (see closed loop description).

20 By synchronized to an event it is meant that the injection timing is substantially linked to the timing of the event; for example the injection is performed at the time of the event, at a predetermined delay after it, or at a predicted time before the event. Such synchronization may allow summing and/or averaging the collected data in a synchronized fashion, similar to gating. Such summing/averaging enables  
25 the analysis and amplification of information related to the desired event, while all events which are not synchronized become "blurred", and have less influence on the final result. For example, an injection profile of once every two seconds allows data accumulated for a dynamic event synchronized to a two second period to be collected and averaged. External interferences, such as breathing, heart motion, and sudden  
30 patient motion, become less influential as they are not synchronized with the two second cycle. Therefore the signal to noise ratio and errors in the reconstructed kinetic parameters are reduced.



Reference is now made to Figure 96, which is a simplified flowchart of a method for measuring kinetic parameters of a radiopharmaceutical in an organ of a body, according to a preferred embodiment of the present invention. The present method differs from the method of Figure 91 in that it images a specific organ of the body. In step 6210, the radiopharmaceutical is administered to the body. In step 6220, the organ is imaged. In step 6230, a model is provided for obtaining kinetic parameters from the imaging is provided. Finally, in step 6240, the kinetic parameters are obtained by applying the measurements to the provided model and extracting the value of the required parameter(s).

A further preferred embodiment of the present invention is a drug formulation for a radiopharmaceutical. Reference is now made to Figure 97, which is a simplified flowchart of a process for obtaining the drug formulation, according to a preferred embodiment of the present invention. In step 6310, kinetic parameters for the radiopharmaceutical are provided. In step 6320, the formulation is determined, based on the provided kinetic parameters. The values of the kinetic parameters are preferably obtained by the method of Figure 91 described above.

In the abovedescribed models C is modeled as a concentration. Alternatively, C may be modeled as a count rate. For each radiopharmaceutical there is a conversion ratio from concentration to count rate which depends on several factors. Factors influencing the conversion may include: mg of matter to number of molecules, the radiopharmaceutical half-life (which determines the average time for a photon to be emitted per molecule), and the rate of isotope decay. If the half-life is short, there is a reduction in available isotopes over the time of acquisition. Modeling the count rate may therefore be easier, and allow later conversion to concentrations.

Commonly, the time for a compound to become widespread in the body is in the time scale of about one minute. Thus the sharp slope in concentration observed immediately following injection lasts only a few seconds before various organs begin uptaking the compound. It is therefore preferable to allow scanning and reconstruction of volumes of interest in a time resolution of about 5-10 seconds. Since the model equations include relatively few parameters, it is assumed that with acquisition of a few minutes long (1, 2, 5, 10 minutes) the number of time points obtained per voxel is in the range of 10-20 (preferably 50 or more), which is expected to enable stable estimation of the kinetic parameters. With radiopharmaceuticals having slower

uptake and release activity it may be preferred to have longer acquisition times, such as 20, 30, or 60 minutes.

The analysis and determination of parameter values may be performed in the time domain, the frequency domain, or in any other transform domain. In the time domain, analysis is performed by solving the differential equation, either analytically or numerically, in order to reach a model which best fits the acquired data. Various numerical tools are known to fit equations of this complexity to a given data set. An example of frequency domain analysis is presented below.

The analytical solution may include integration over the input  $C_g$ , which may not be available with sufficient accuracy. In such cases, numerical methods for fitting the differential equations may prove more stable and accurate.

It is expected that frequency domain analysis will be particularly effective when the data is acquired in a frequency representation. It is expected that time domain analysis will be particularly effective when the data is obtained over time. Alternative approaches may be tested by converting the data from one form to the other, and the more stable approach may be selected.

In some cases, the model above may further include interstitial volume, so that substances move from capillaries to the interstitial domain and from there to the cells, and vice versa. Transfer to and from the interstitial domain may be added to the equations. In many cases the difference in concentration between the interstitial volume and the capillaries is insignificant, thus they may be modeled as one domain.

It should be noted that the general blood concentration,  $C_g$ , may differ from one location to another, for example between veins and arteries. Therefore, it may be preferable to measure the blood concentration by a sample from the arteries or by measuring the concentration inside the left chambers of the heart.

Similarly, in the case of cardiac imaging there might be poor blood flow along one or more of the coronary arteries, and thus uptake of substance by cells in one voxel might reduce the remaining concentration in the artery available for voxels further along the given artery. Thus the value of  $C_g$  may actually be lower for the more distal voxels. Changes in the value of  $C_g$  may be handled by iterating the parameter estimation while correcting the  $C_g$  value once the uptake in the more proximal voxels has been estimated.

Note that if the radiopharmaceutical administration is based on a periodic injection protocol, the concentration in the general blood pool (either arterial or venous) may respond in a periodic pulsatile profile, which has a harmonic spectrum.

Following is a discussion of the application of frequency domain analysis to the abovedescribed voxel dynamic modeling. Frequency domain analysis allows the use of techniques for measuring the frequency response to a periodic injection protocol, similarly to the way frequency response is evaluated in passive electrical circuitries. For example, the frequency response may be measured by injecting the radiopharmaceutical several frequencies, and then determining the amplitude of the response at a given frequency, the phase response, or the comparative amplitudes at several frequencies. The results are then compared with the model of the frequency response and parameters of interest are extracted (e.g. resistors and capacitor values in electrical circuitry, or diffusion coefficients and blood flow,  $F$ , in the voxel dynamic model).

Taking model 3 as an example, the Fourier transform equivalents of Equations 10-12 are:

$$C = (C_t \cdot V_t + C_b \cdot V_b) / V = C_b \cdot R_b + C_t \cdot (1 - R_b) \quad (18)$$

$$j\omega C_t = K_{in} \cdot C_b - K_{out} \cdot C_t \quad (19)$$

$$j\omega C_b = \frac{F}{V_b} (C_g - C_b) - K_{in} \cdot C_b + K_{out} \cdot C_t \quad (20)$$

where  $C$ ,  $C_b$ ,  $C_t$ ,  $C_g$  are in the frequency domain,  $\omega$  is the angular frequency, and  $j$  is the imaginary unit,  $\sqrt{-1}$ ).

Equations 18-20 result in Equation 21, which relates the concentration in the voxel of interest ( $C$ ) to the concentration in the arterial blood ( $C_g$ ) in the frequency domain:

$$C = \frac{\frac{F \cdot C_g}{V} \left[ \frac{V_t}{V_b} + \frac{j\omega + K_{out}}{K_{in}} \right]}{\left( j\omega + \frac{F}{V_b} + K_{in} \right) \cdot \left( \frac{j\omega + K_{out}}{K_{in}} \right) - K_{out}} \quad (21)$$

The relationship between C and C<sub>g</sub> can be measured in several frequencies, enabling the extraction of F, K<sub>in</sub>, and K<sub>out</sub>.

Equation 21 is useful for analyzing the value of the kinetic parameters. Consider the case of  $\omega \ll K_{out}$ , that is the case in which rate of clearance is much faster than the rates of changes in the blood flow. In practice, it is difficult to obtain  $\omega \ll K_{out}$  for some radiopharmaceuticals, requiring slow and controlled changes in the blood concentration.

For  $\omega \ll K_{out}$ , Equation 21 becomes:

$$\frac{C}{C_g} = \frac{\frac{F}{V} \left[ \frac{V_t}{V_b} + \frac{K_{out}}{K_{in}} \right]}{\left( j\omega + \frac{F}{V_b} \right) \cdot \left( \frac{K_{out}}{K_{in}} \right)} = \frac{F}{V} \cdot \frac{\frac{V_t \cdot K_{in}}{K_{out}} + V_b}{j\omega V_b + F} \quad (22)$$

Equation 22 provides a highly important relationship, as the ratio between two measurements, each with two different low frequencies  $\omega_1$  and  $\omega_2$  (i.e. two slow derivatives of concentration changes), provide a direct measure of flow rate:

$$\frac{\left( \frac{C}{C_g} \right)_2}{\left( \frac{C}{C_g} \right)_1} = \frac{j\omega_1 \cdot V_b + F}{j\omega_2 \cdot V_b + F} \quad (23)$$

The ability to isolate parameters, so that the values of different parameters do not affect each other, is of high importance. Parameter isolation combined with the high sensitivity and the ability to produce multiple repetitions in different frequencies

or slopes may enable extracting some parameters in a quantitative and efficient manner.

Quantification in the case of  $w \ll K_{out}$  depends on the prior estimation of the partial volume in each voxel containing the blood compartment. Once  $F$  is known,  
5 the ratio of  $K_{in}/K_{out}$  is obtainable from the Equation 22 above.

In a more typical scenario,  $w \gg K_{out}$ , and equation 21 becomes:

$$\frac{C}{C_g} \cong \frac{F}{V} \cdot \frac{K_{in} \cdot V_t + jw \cdot V_b}{jw (jw \cdot V_b + K_{in} \cdot V_b + F)}$$

(24)

10

For  $w \gg K_{out}$ , measuring the ratio of  $C/C_g$  in multiple frequencies allows the recovery of the flow  $F$  and the wash-in rate  $K_{in}$  (which is associated with the well being of the cells) in a quantitative manner.

It is possible to perform all analyses in terms of the absolute amplitudes of  $C$   
15 and  $C_g$  by converting the modeling equations (which include complex numbers) to absolute numbers. Alternatively, phase analysis may be used. An additional alternative is to transform time-domain signals into the frequency domain with the Fourier transform, and to perform the remaining analysis in the frequency domain.

## 20 Global Zero:

The following relates to a plurality of independently moving detectors, which move independently during data acquisition.

Since each detector is associated with one or several motors, the different motors have to be referenced to a single zero point, with an accuracy, which is greater than that of  
25 a desired object size for detection. For example, the accuracy may need to be better than about 10% of the object size, and preferably 1%, or even 0.1% of the desired object size for detection.

In accordance with a first global zero embodiment, the various detectors are referenced to a single location, for example, a hot wire, as a radiation reference point  
30 of a known position. However, this requires that the position of the radiation reference point be known with a very great accuracy, which is in itself difficult.

In accordance with a second global zero embodiment, relative measurements of at least two and preferably, at least three radiation reference points are performed, by the detectors, moving independently, and a global zero point is determined from the relative measurements, using dedicated algorithms developed for the purpose. This  
5 bypasses the need for the exact position of the reference source of the first global zero embodiment and decreases uncertainties.

#### **Pixel Sensitivity Map:**

The evenly illuminated board used by present day Anger cameras for  
10 obtaining a pixel sensitivity map is inapplicable for the radioimaging cameras of the present invention, as described for example, in Appendix A, due to their curvatures. Yet, producing a sensitivity map for each detector or assembly, individually, is very time consuming. Given a structure of at least 10 assemblies, this may require 10 individual sensitivity maps.

15 In accordance with embodiments of the present invention, a hot wire of substantially even illumination is used as a radiation reference point, for obtaining a sensitivity map of the all detectors – that all detecting units or detecting pixels, simultaneously - in parallel. This is done by performing measurements of the evenly illuminated wire with the plurality of detectors, each from its respective position and  
20 orientation, and comparing the sensitivity of each detector, after correcting for distance and viewing angle of each.

#### **Pixel and Collimator Integrity check:**

The method of performing a pixel sensitivity map is further applicable for  
25 ensuring the integrity of the pixels and their collimators, simultaneously, for all pixels. A large discrepancy in the readings will suggest that there may be a structural problem, for example, a broken collimator, a chipped detector, or a broken electrical connector.

#### **Detecting Patient's Motion:**

30 Present day Anger cameras generally view enough of the body to have several reference edges in the image, so that patient's motion is immediately seen. But the radioimaging cameras of the present invention, for example, as described in Appendix



A, view a very small region of the patient's body, with little to use as a point of reference, so patient's motion may not be apparent.

In accordance with a first embodiment, the acquisition time for a full image is divided to  $N$  periods, where  $N \geq 2$ , and  $N$  full images are acquired, each for  $1/N$  of the time. The  $N$  images are then compared by various methods, to determine if the two or more images are different, for example, by using a statistical technique. If the images appear to have come from different distributions, new images may be taken.

Additionally or alternatively, panoramic views may be constructed from the  $N$  images, which include superposition of about 90% or so. The panorama is a method of display that enables to easily identify objects in the raw data, and the difference between panoramic views of different acquisition slices provides the information on possible patient's movement.

#### **Temporal Resolution:**

In accordance with a first embodiment of the present invention, a CZT module contains 256 pixels of a CZT detector, the 256 pixels being associated with 2 ASICS, each ASIC receiving photon count events from 128 pixels.

It will be appreciated that a smaller number of pixels may be associated with a single ASIC, for example, 64, or 32, or another number, as desired.

The solid-state CdZnTe (CZT) detector may be obtained, for example, from eV Products, a division of II-VI Corporation, Saxonburg Pa., 16056, or from IMARAD IMAGING SYSTEMS LTD., of Rehovot, ISRAEL, 76124, [www.imarad.com](http://www.imarad.com), or from another source.

The ASIC may be, for example, OMS 'XAIM3.4' made by Orbotech Medical Systems, Rehovot, Israel, together with the CZT detector.

In accordance with a first embodiment, the 2 ASICS share a common output and transmit the data to an ADC printed circuit board (PCB) that handles in parallel 4 CZT modules. Thus, a total of 1024 pixels may be channeled through one ADC board, forming an assembly.

In accordance with a second embodiment, the 2 ASICS may be channeled to a single ADC.

In accordance with a third embodiment, a single ASICS may be channeled to a single ADC.

A potential bottle neck in the processing of events is the ASICs of the CZT module and their connection to the ADC PCB.

In accordance with the first embodiment, an ASIC of 128 pixels can process one photon hit within 3.5  $\mu$ s, or 285,000 events/s over 128 pixels, i.e. over 2200 events/pixel/s – which is an exceedingly high rate.

The 2 ASICs share the same output, and hence coincident event output of the 2 ASICs in a CZT module will cause a collision and information loss. The duration of an event output from the ASIC is 1  $\mu$ s.

It will be appreciated that the number of events/pixel/s may be increased by associating fewer pixels with each ASIC. For example, given 32 pixels per ASIC, that number may be increased by a factor of 4, to 8800 events/pixel/s.

It will be appreciated that coincident event information loss may be further reduced by associating each ASIC with a single output.

The embodiments thus described provide high temporal resolution since there is no smearing of the timing of events - no merging of the timing of events in a buffer, and little loss due to coincidence counts.

In accordance with another embodiment, a buffer may be used, but with a time stamp, for example, as follows: the ASIC has an independent channel of analog pulse processing for each pixel. Each channel is event triggered and contains a low-noise preamplifier, pulse shaper, amplifier, peak-and-hold circuitry. The ASIC also provides selectable gain, threshold, shaping time, hold time and readout delay within the hold window. These parameters are judiciously varied to achieve optimum performance for a given photon energy range and event rate. The ASIC generates energy and position information as well as an event trigger for each gamma event.

Common to all pixels served by the ASIC is a control logic block and a buffered multiplexed readout. Such control and readout circuitry provides the means to control the ASIC and to output the photon event data. A time stamp mechanism along with the buffer associates each event with a specific time of arrival, to provide temporal resolution.

### **Independent Temperature Control for the Plurality of Detectors:**

Solid state detectors, such as CdTe and CZT, are susceptible to leakage currents, which are temperature dependent. Often, thermoelectric coolers are employed, based

on Pelletier cooling. A single stage thermoelectric cooler can reduce the leakage current by a factor of approximately 100. Natural or forced convection may be further used, to provide a heat sink to the thermoelectric coolers.

Yet, when using a plurality of independently moving detectors, uniform temperature  
5 may be required in order to provide uniformity in the drift current, hence the energy window. Since the heat is primarily produced by the electronics, the higher the count rate of a detector, the higher the heat generation, and detectors that experience a high count rate will operate at a higher temperature than those of a low count rate, leading to a shift in the drift current hence energy window of the detector.

10 Nonetheless, solid state detector systems that are currently employed do not address the issue of uniform temperatures across the plurality of detectors.

In accordance with the present invention, a CZT module containing the solid state detector, such as a CZT detector, is pixilated, to form a detector array or a block, and associated with a dedicated ASIC.

15 Preferably, each CZT module includes a detector block and the associated ASIC is independently monitored for temperature, by a temperature sensor, which reports to a controller, for providing thermoelectric cooling, responsive to the temperature sensor's input.

Alternatively, each CZT module includes two or more detector blocks, associated  
20 with the dedicated ASIC and are monitored as a single unit for temperature, by the temperature sensor, which reports to the controller, for providing thermoelectric cooling, responsive to the temperature sensor's input.

The number of pixels in the CZT Module may be, for example, as low as 10, or as high as 1000, as required.

25 In accordance with another embodiment, no temperature sensor is required. Rather, the Pelletier cooling is applied to a CZT module, responsive to the count rate from that module.

It will be appreciated that other solid state crystals, for example, CdTe or another may be used.

30

### **Spectral Resolution:**

In accordance with embodiments of the present invention, the bias and current may be monitored and controlled per 1024 pixels, channeled through an ADC board, and

forming an assembly, thus further monitoring and controlling the energy window, and ensuring uniformity of the energy window amongst the different assemblies.

It will be appreciated that the bias and current may be monitored and controlled on the basis of each CZT module or on the basis of each ASIC, where desired. It will be further appreciated that the monitoring and correcting may be dynamically performed, in real time.

#### **Non-Uniform Scanning and Reconstruction:**

In accordance with embodiments of the present invention, the radioimaging cameras described in Appendix A and other radioimaging cameras of independently moving detectors, wherein the detectors move independently during data acquisition, may further employ non-uniform scans.

A scanning density may be defined by the angular and translational increment size, or steps, the smaller the increment, the higher the density.

Additionally, the scanning density may be defined by the acquisition time at each position - the longer the time, the higher the density.

The non-uniform scans may relate to non-uniform angular steps of the detector along a sweep, non uniform detector translational steps, or different steps by different detectors. Some detectors may employ dense steps and others may employ sparse steps, for example, based on active vision, as taught in Appendix A, hereinbelow.

A control system may adapt the density of the scan to the distance to the object of interest. Since resolution decreases with distance, the higher density may compensate for increased distance.

Additionally or alternatively, the angular steps may increase in density when scanning the region of interest, and decrease in density, when scanning other regions.

Furthermore, more than one region of interest may be scanned with dense steps, simultaneously. The two regions of interest may be, for example, a tissue region and a blood pool region. This has applicability, for example, to dynamic studies of blood perfusion, by providing even scanning resources both to the blood and to the tissue.

Scanning resources include, for example, detector dwell time, number of detectors, angular and translational increments, and the like - features that increase the amount of data collection.

Additionally, convex scans may be employed.

Variable scans, where a same region is scanned first with a first density and then with another density, may be employed.

Alternatively, a same region may be scanned by a first group of detectors with a first density and then by a second group of detectors with another density, concurrently, or  
5 at different times.

This means that a same region is scanned with at some density by a given detector and at a different density by another detector.

Furthermore, in accordance with embodiments of the present invention, non-uniform reconstructing may be employed, providing non-uniform resolution, so that the  
10 resolution increases with the stability, hence reliability, hence reliability of the data.

The non-uniform reconstruction employs a condition number, which is a measure of a stability, hence reliability, hence reliability of a matrix to numerical operations, and is defined as:

$$[1] \quad \kappa(A) = \|A\| \cdot \|A^{-1}\|$$

15

If a matrix has a large condition number, for example, larger than 1000 then there is a possibility that even a small error in the data will lead to a large error in the solution.

The inaccuracies in the data will always be present because all measurements are finite and because all computers have a finite precision. Hence it is important to be on  
20 guard whenever solving ill-conditioned equations. Furthermore, it is ill advised to spend detecting time and other scanning resources in acquiring data that will lead to erroneous results due to instability, hence reliability.

In the present example, count data is processed to reconstruct the intensity distribution within voxels of measured volume.

25 In general, we assume an intensity distribution,  $I$ , defined over an input space  $U$ , where  $U$  comprises a set of basic voxels in a three dimensional space, and  $I(u)$  defines the radiation intensity of a basic voxel  $u \in U$ . A detecting pixel, positioned on the radioimaging camera takes a series of measurements  $\mathbf{y} = (y_i)_{i=1}^T$  from different positions and orientations around the volume  $U$ . The geometrical and physical  
30 properties of the detecting pixel, together with its position and orientation for the given measurement, determine the detection probability  $\phi_i(u)$  of a photon emitted

from the voxel  $u$ . Thus the effective intensity of location  $u$  as viewed by the detecting unit during measurement  $t$  is  $\phi_t(u)I(u)$ .

The random count  $X_t(u)$  of photons that are emitted from location  $u$  and detected in measurement  $t$  is modeled by a Poisson process with a mean  $\phi_t(u)I(u)$ . The total count  
5 of photons detected in measurement  $t$  is:

$$[2] \quad Y_t = \text{Poisson} \sum_{u \in U} \phi_t(u)I(u)$$

The reconstruction problem is to reconstruct the intensities  $(I(u))_{u \in U}$  from the  
10 measurements  $(y_t)_{t=1}^T$ .

Applying equation [1] to the detection probability matrix  $\phi_t(u)$ , it is possible to evaluate the condition number, hence the measure of stability, hence reliability of the various voxels  $u$ .

When the condition number for a particular voxel  $u$  is around 1, or no greater than 10,  
15 it is advisable to invest scanning resources, and apply dense scanning, and even subdivide the voxel to finer voxels. Thus, non-uniform scanning may be a function of the condition number.

Additionally or alternatively, when the condition number for a particular voxel  $u$  is greater than 100, or even greater than 1000, reconstruction is unstable and sensitive to  
20 noise. So it may be advisable to do with sparse scanning and even merge several voxels, to a larger voxel. Alternatively, denser scanning may be employed in order to increase the condition number of the voxel.

In accordance with embodiments of the present invention, there are several ways of utilizing the condition number, to direct and employ scanning resources, as follows:

- 25 1. add regularization factors (e.g. smoothness constraint, or piecewise smoothness constraints - for edge preservation) or add assumptions to the data (e.g. the range of realistic values per voxel should be, for example, no less than 0 and no greater than a predetermined value, or assume a distribution of counts per voxel, such as gamma distribution, based on typical spatial structures, and the like).
- 30 2. define a resolution in each region according to the information provided to that region- for example, if there are 1000 different views independently covering 1 cubic cm and almost not affected by the surrounding, then theoretically that volume can be



divided up to about 1000 voxels (e.g. 1mm square each), if the views create linearly independent set of equations with high condition numbers.

3. if that information is ill-conditioned (less views or views which are practically not

5 independent), then one can decide to divide that volume to fewer voxels. Some approaches can be taken in this case, as follows:

- i. use regularization only in regions which are ill-conditioned.
- ii. with regard to neighboring voxels with poor reliability, they may be merged into bigger voxels, thus increasing their reliability to the combined one.
- 10 iii. point (ii) can be carried out repeatedly on the lowest reliability voxel - merge it with one of the neighboring voxels to form one bigger voxel, to form an aggregate of voxels, until no voxel is left with a reliability below a threshold. It will be appreciated that the aggregate voxels have a lower resolution locally since there is not enough resolution to support splitting, but all other regions with good coverage
- 15 remain of high resolution, according to their coverage.
- iv. the principle of (ii) can be reversed: define the whole volume as a single huge voxel, and split it to form sub-voxels – as long as each voxel maintains enough reliability, then repeatedly divide each voxel as long as the result of such split will maintains reliability high enough for stable results. This process produces a quad-
- 20 tree, in multi scale of resolutions. The definition of the voxels can be determined in advance, based on the scan pattern, regardless of the count reading from the detectors.
- v. same as (iv), but with adaptation of the scanning pattern, when a region is interesting but is still left with coarse resolution, so as to allocate more scanning resources, such as dwell time, number of detectors, angular and translational
- 25 increments, to cover that region and to form more independent views such as to increase the reliability of the reconstruction of that area. This can still be done before data (detectors counts) is collected.
- vi. same as (iv), but with multi-resolution as part of the reconstruction:  
starting with reconstructing equations relating to the entire volume as a single
- 30 voxel, performing iterations where the volume is split, while taking the previous iteration as initial condition, and selecting the stable split. Then repeating the splitting of some of the voxels, for which reconstruction is reliable and perform reconstruction

for them, and over again, until reaching a split, which is no longer stable, thereby arriving at the final resolution for that location.

vii. items (v) and (vi) may be combined, by adapting a scanning pattern, not only to enable stability, hence reliability and reliability in reconstruction, but also to improve reconstruction. For example, if the reconstruction from the data, for example, based on item (vi) produced a split of is 1 cm resolution, then additional scanning in that region of interest may allow additional information to reach higher resolution, and further splits, thus improving the resolution in that region of interest.

#### 10 **Two Step Imaging for Dynamic Studies, Based on Anatomic Region of Interest:**

In accordance with embodiments of the present invention, two-step protocols are proposed to enable anatomic modeling of small regions of a target.

As a first step, conventional injection and imaging is performed, using standard voxel division, for example, of 5 X 5 X 5 mm, to obtain an image of the target, for example, the heart.

An anatomical region of interest is then defined on the image, and a new voxel map is generated, along the anatomical boundary lines. The anatomical region of interest may be a small portion of the overall image.

As a second step, a second injection is made, followed by scanning with detecting recourses aimed at the anatomical region of interest.

In a way, this approach is suggestive of a zooming in approach, for example, as taught in commonly owned PCT/IL2005/001173. But there, voxel reconstruction was rigorous throughout, and here, the first step employs cubical voxels, as known, but these are used to define anatomical voxels for the second step.

Several radioimaging protocols may be employed for this purpose, for example, described as protocol J2 of Figure 101D and 101E, as follows:

Step 1: a first injection, for example, a single bolus of a first marker, such as Tl-201, at a low dose of between 0.5 and 2 mCi, and imaging the heart for example, for about 1 minutes, to acquire a high quality image, to be used for constructing the anatomical image, and for defining a finer region of interest; and

Step 2: while the patient is immobile, injecting 20-40 mCi, preferably of a second marker, for example, Tc-99m-sestamibi, and performing an up to 10 minute

dynamic study, with image reconstruction every several seconds, for example, every 5 or 10 or 20 seconds, the dynamic image being superimposed on the first image.

On the one hand, when the image reconstruction is anatomically defined, the number of variables decrease drastically, for example, by a factor of 10;

5 Additionally, where only a small anatomically defined region is of interest, the scanning sweep is considerably shortened.

Both these factors together reduce the scanning time necessary for obtaining informative images for the anatomically defined region of interest.

10 In consequence, the two step rigorous-to-anatomic protocol is a highly effective technique for dynamic studies, providing anatomically reconstructed data, at very short time intervals of several seconds, and enabling the acquisition of kinetic parameters of specific tissues and across different tissues.

It will be appreciated that other markers may be used, and for other durations, provided the basic scheme of a first image for defining the anatomical boundaries, and  
15 the second image for dynamic reconstruction of anatomical voxels is maintained.

### **Obtaining Kinetic Parameters:**

Dynamic studies, aimed at obtaining kinetic parameters require the acquisition  
20 of full reconstructed images at a rate that is no greater than about half the frequency of the sampled kinetic parameter. For example, if blood circulates throughout the body in about 1 minute, than sampling of that process should take place at least twice per minute. Preferably, sampling should be at a much greater frequency, for example, at least 6 times per minute, for example, every 10 seconds.

25 Furthermore, in order to obtain fully reconstructed images every 10 seconds, detector time slots must be much smaller, for example, a fraction of a second.

Figure 98 illustrates counts obtained every 1/1000 of a second, to be used for image reconstruction, for example, every 5 seconds, as seen in Figure 2A, hereinbelow.

30 Additionally, based on Garcia et al. (Am. J. Cardiol. 51<sup>st</sup> Annual Scientific Session, 2002), dynamic studies are best performed within about the first 100 seconds after injection, or within the first 60 seconds after injection.

Such studies are possible, when temporal resolution is available, as described hereinabove, and when scanning resources are directed at a specific and small anatomic region, for example, as described in conjunction with the section: Two Step Imaging for Dynamic Studies, Based on Anatomic Region of Interest.

5

### **Experimental Results**

Experimental results, in accordance with embodiments of the present invention are provided in Figures 101A – 101H.

Figure 101A shows image full cardiac image acquisition in 5 seconds, 10  
10 seconds, 15 seconds, and up to 240 seconds, showing the improvement of the image, with increased imaging time.

Nonetheless, Figure 101A illustrates that reasonable images, for example, for a two step image acquisition protocol J2 described hereinabove, in conjunction with the section: “Two Step Imaging for Dynamic Studies, Based on Anatomic Region of  
15 Interest,” can provide meaningful results.

Figure 101B illustrates contouring, which may be used for defining anatomical boundaries.

Figure 101C illustrates a dual isotope image, of a 2 cm Tc-99m insert in a Tl-201 window image, wherein it is apparent that the Tc-99m insert is not visible in the  
20 Tl-201 window, confirming the spectral resolution of the camera.

## **EXAMPLE 16A**

### ***Early Imaging Protocols***

25 Due to the very fast acquisition time of the camera disclosed in U.S. Pat. Appl. No. PCT IL2006/000059 assigned to Spectrum Dynamics LLC, the present invention contemplates the use of early imaging protocols. Such protocols comprise imaging an area of interest (e.g. heart) immediately following injection of a radiopharmaceutical. The image is obtained whilst the radiopharmaceutical is still being distributed i.e.  
30 during a dynamic process, and is not at full strength in the liver. In this way it is possible to capture a process whilst it is still changing. Not only do early imaging protocols capture physiologically relevant images not available using traditional protocols, but also the length of time of the protocol is significantly shorter. Thus,

typical times for such protocols may comprise about 30 minutes, or more preferably about 20 minutes in total. This is of benefit to the practitioner (frees up camera time) as well as to the patient. Furthermore, the imaging time using the camera of the present invention is also shortened to a time of about 6 minutes, preferably 3 minutes and even more preferably less. Using early imaging, it is conceivable to image a mild stenosis in the arteries since such an effect should be detected using a system which incorporates dynamic kinetic parameters. The ability to image a stenosis using an early imaging protocol is illustrated in Figures 102A-B. The images produced may be 3D spectrum images.

It will be appreciated that since the uptake process is still changing immediately following injection, images may be scanned at multiple time points throughout an early imaging protocol providing a more thorough and complete view of the organ of interest. In addition kinetic data (e.g. slope and viability) may be obtained by measuring at multiple time points.

Early imaging protocols may be used to detect radiopharmaceuticals whilst the patient is at rest and/or following a stress (physical or pharmaceutically induced). In addition the protocols described herein may be effected under the camera.

It will be appreciated that early imaging requires accurate control of timing. Accordingly, the present invention anticipates an automated early imaging protocol including an automated administration device configured to perform intravenous (IV) injection, intramuscular (IM) injection, subcutaneous injection, transdermal application, oral administration, nasal administration, inhalation, transcervical application, transrectal administration, or another type of administration known in the art. In addition, the present invention anticipates a kit for early imaging comprising at least one syringe of radiopharmaceutical (For example, thallium, sestamibi, myoview or cardiotec) and a syringe with saline. It will be appreciated that kits for stress protocols will typically comprise two syringes of radiopharmaceuticals, the first to be injected at rest and the second during peak stress. The radiopharmaceuticals may or may not be identical (see example 17A herein below). The syringe injected at rest typically comprises a radiopharmaceutical at a low dose (e.g. if the radiopharmaceutical is Tc99, then less than 6 mCi) whereas, the syringe injected during peak stress typically comprises a radiopharmaceutical at a high dose (e.g. if the radiopharmaceutical is Tc99, then between 25-50 mCi) so that interference between

the rest and stress radiopharmaceutical is minimal. Exemplary pairs of radiopharmaceuticals include Tl201 and Tc99; Tl201 and Iodine123 and Tc99 and iodine 123. An exemplary single radiopharmaceutical that may be used in accordance on the present invention is Tc99. The kit may also comprise a syringe with a pharmaceutical agent that induces stress such as adenosine and also a syringe comprising saline.

In order for the protocol to be automated, it is preferable that the kit comprises an identification tag for the patient (e.g. a bracelet) which corresponds to an identity tag on the syringes of the kit of the present invention. The identity tag of the syringe is encrypted with all the protocol parameters ensuring that the whole imaging process is entirely automated. Exemplary identification tags include, but are not limited to a RFID tag, smart card, memory card (such as a disk-on-key (e.g., a USB key)), compact disc, minidisk, disposable computer-readable medium, or other electronic memory. An exemplary early imaging protocol is described in Table 91 herein below.

Table 91

Description: Early mibi mibi imaging  
Indication: myocardial perfusion

20

<i>Length of Time</i>	<i>Patient flow</i>	<i>Radiopharmaceutical</i>	<i>Dose (mCi)</i>	<i>Mode of administration</i>	<i>Acquisition parameters (detector; windowing, etc.)</i>	<i>Clinical parameters acquired after processing</i>
	Injection	Tc99m Sestamibi	low dose for example 8-12	Bolus IV		
7 minutes	waiting					
5 minutes	Imaging					
2 hours	waiting					
Variable (2-10 minutes)	Stress				Physical or pharmacological	
	Peak stress injection	Tc99m Sestamibi	medium - highdose for example 24-36	Bolus IV		
0 - 2 min	imaging					Heart perfusion

Timeframe summary:



Total patient time – up to 2.5 hours

Early, immediate post injection SPECT imaging is not feasible with current SPECT technology because:

1. the prolonged acquisition time cannot be completed within the first minutes after tracer injection, typical current standard SPECT acquisition times are around 12.5-15 minutes.
2. the prominent uptake of the tracer in the liver in the very first minutes after injection generally obscures the inferior myocardial wall. Therefore, using standard SPECT systems, image acquisition is not commenced until 45-60 minutes after injection to allow for clearance of the radiotracer from the liver.

These obstacles may be overcome using the system of the present invention by:

1. capitalizing on the system's markedly improved sensitivity allowing acquisition completion in just 2 minutes
2. exploiting the system's ability to acquire SPECT studies with the patient sitting upright, thus having their liver descended to more caudal position and not interfering with the sampling the inferior myocardial wall, even at the earliest stages when it contains high levels of radioactivity

#### EXAMPLE 17A

##### *Simultaneous Dual isotope protocol*

Currently there are difficulties in implementing a methodology based on simultaneous dual isotope detection with present technologies because the energy resolution of the conventional SPECT cameras allows for too much "crosstalk" between the two isotopes. Various crosstalk correction methods of varying complexities and results were advised [Okudan B, Smitherman TC. Anadolu Kardiyol Derg. 2004 Jun;4(2):161-8. Review. PMID: 15165953; Weinmann P, et al., Eur J Nucl Med Mol Imaging. 2003 Jan;30(1):25-31. Epub 2002 Oct 19. PMID: 12483406; Ohyama Y, et al., Radiat Med. 2001 Mar-Apr;19(2):81-7. PMID: 11383647; Hannequin P, et al., J Nucl Cardiol. 2001 Mar-Apr;8(2):144-51. PMID: 11295691; Knesaurek K, Machac J. Br J Radiol. 1999 Sep;72(861):872-81. PMID:

10645193; Kiat J Nucl Med. 1994 Apr;35(4):542-8. ID: 8151372], which precluded the routine application of simultaneous dual isotope myocardial SPECT.

The present inventors have shown that it is possible to perform a simultaneous dual isotope protocol using a high photon energy isotope (e.g. sestamibi) and a low photon energy isotope (e.g. thallium) provided that the high photon energy isotope is administered at a low enough dose so that it does not interfere with the low photon energy isotope. The camera used according to embodiments of the present invention provides far better energy resolution and sensitivity, thereby providing better energy discrimination of the two isotopes and mitigates the isotope crosstalk phenomenon in the first place (see Figures 103A-B). Table 92 summarizes an exemplary ultra-fast simultaneous dual isotope protocol.

**Table 92**

Description: ultra-fast simultaneous dual isotope

Indication: myocardial perfusion

15

<i>Length of Time</i>	<i>Patient flow</i>	<i>Radiopharmaceutical</i>	<i>Dose (mCi)</i>	<i>Mode of administration</i>	<i>Acquisition parameters (detector; windowing, etc.)</i>	<i>Clinical parameters acquired after processing</i>
	Injection	Tc99m Sestamibi	low dose for example Up to 10	Bolus IV		
Variable (2-10 minutes)	Stress				Physical or pharmacological	variable
	Peak stress injection	Thallium-201	Medium dose for example 3	Bolus IV		
0 - 10 min	imaging				Energy window 3-15%	heart perfusion

Timeframe summary:

Total patient time – up to 20 minutes

Clinical protocol advantages:

This protocol can register stress and rest images. Patient interphases with the system only once.

20

According to this protocol, the myocardium is stained with two different myocardial perfusion tracers based on two different radioisotopes, emitting gamma rays of different energies, one at rest ( $^{99m}\text{Tc}$ -MIBI for example) then another one

(<sup>201</sup>Tl) during peak exercise. Only one acquisition is performed, simultaneously acquiring both radioisotope signals and separating them by multiple energy windows tuned to each isotope emission energy respectively.

Advantages:

1. Camera time per patient is halved.
2. The Stress/Rest study pairs are inherently and perfectly registered eliminating artifacts originating from inconsistent positioning and reorientation of the two series acquired separately.

### EXAMPLE 18A

#### *Simultaneous Dual Isotope Acquisition with a camera according to an embodiment of the present invention*

##### *Proof of Concept Phantom Study*

A Comparison of perfusion defect (2cm cold insert) from Tl-201 images obtained with simultaneous dual isotope acquisition (ie. Tl-201 contaminated with Tc) to “virgin” Tl-201 acquisition is presented in Figures 104A-B using a standard camera (A-SPECT) – GE Millenim VG or a camera according to the embodiments of the present invention (D-SPECT). Experimental procedures for the experiment detected by the camera according to embodiments of the present invention are presented in Figure 105. Experimental procedures for the experiment detected by the standard GE Millenium camera are presented in Figure 106. Further results are described in Figures 107-110A-B. As can be seen from Figures 107-110A-B the camera of the present invention was able to obtain clear images, and could detect the area of ischaemia using dual isotopes. In sharp contrast, the standard camera could not obtain clear images and the area of ischemia as obtained using dual isotopes was very hard to detect due to interference between the two isotopes.

It is appreciated that certain features of the invention, which are, for clarity, described in the context of separate embodiments, may also be provided in combination in a single embodiment. Conversely, various features of the invention, which are, for brevity, described in the context of a single embodiment, may also be provided separately or in any suitable subcombination.

Although the invention has been described in conjunction with specific embodiments thereof, it is evident that many alternatives, modifications and variations will be apparent to those skilled in the art. Accordingly, it is intended to embrace all  
5 such alternatives, modifications and variations that fall within the spirit and broad scope of the appended claims. All publications, patents and patent applications and GenBank Accession numbers mentioned in this specification are herein incorporated in their entirety by reference into the specification, to the same extent as if each individual publication, patent or patent application or GenBank Accession number  
10 was specifically and individually indicated to be incorporated herein by reference. In addition, citation or identification of any reference in this application shall not be construed as an admission that such reference is available as prior art to the present invention.

## WHAT IS CLAIMED IS:

1. A method of radioimaging a myocardial perfusion, the method comprising in sequence:

- (a) administering to a subject about 3 mCi Tl201 thallous chloride;
- (b) allowing said subject to rest;
- (c) radioimaging a heart of said subject;
- (d) subjecting said subject to a physical stress;
- (e) administering to said subject at a peak of said physical stress about 20-30 mCi Tc99m sestamibi; and
- (f) radioimaging said heart of said subject, thereby radioimaging a myocardial perfusion.

2. The method of claim 1, comprising at least one or more of the following:

- (1) step (b) is for about 10-15 minutes;
- (2) step (c) is for about 2 minutes;
- (3) step (d) is effected about 2 minutes following step (c);
- (4) step (f) is effected about 30-60 minutes following step (d); and
- (5) step (f) is for about 2 minutes.

3. The method of claim 1, effected as described in Table 1.

4. A method of radioimaging a myocardial perfusion, the method comprising in sequence:

- (a) administering to a subject about 8-10 mCi Tc99m sestamibi;
- (b) allowing said subject to rest;
- (c) radioimaging a heart of said subject;
- (d) subjecting said subject to a physical stress;
- (e) administering to said subject at a peak of said physical stress about 20-30 mCi Tc99m sestamibi; and
- (f) radioimaging said heart of said subject, thereby radioimaging a myocardial perfusion.

5. The method of claim 4, comprising at least one or more of the following:

- (1) step (b) is for about 30 minutes;
- (2) step (c) is for about 2 minutes;
- (3) step (d) is effected immediately following step (c);
- (4) step (f) is effected about 30-60 minutes following step (e); and
- (5) step (f) is for about 2 minutes.

6. The method of claim 1, effected as described in Table 2.

7. A method of radioimaging a myocardial perfusion, the method comprising in sequence:

- (a) administering to a subject about 3 mCi Tl201 thallous chloride;
- (b) allowing said subject to rest;
- (c) radioimaging a heart of said subject;
- (d) subjecting said subject to a pharmacological stress;
- (e) administering to said subject at a peak of said pharmacological stress about 20-30 mCi Tc99m sestamibi; and
- (f) radioimaging said heart of said subject, thereby radioimaging a myocardial perfusion.

8. The method of claim 7, comprising at least one or more of the following:

- (1) step (b) is for about 2 minutes;
- (2) step (c) is for about 2 minutes;
- (3) step (d) is effected immediately following step (c);
- (4) step (e) is effected about 2 minutes following step (d);
- (5) step (f) is effected immediately following step (e);
- (6) step (f) is for about 2 minutes; and
- (7) said pharmacological stress is adenosine or dipyridamole;

9. The method of claim 7, effected as described in Table 3.



10. A method of radioimaging a myocardial perfusion, the method comprising in sequence:

- (a) administering to a subject about 8-10 mCi Tc99m sestamibi;
- (b) radioimaging a heart of said subject;
- (c) subjecting said subject to a pharmacological stress;
- (d) administering to said subject at a peak of said pharmacological stress about 20-30 mCi Tc99m sestamibi; and
- (e) radioimaging said heart of said subject, thereby radioimaging a myocardial perfusion.

11. The method of claim 10, comprising at least one or more of the following:

- (1) step (b) is immediately following step (a);
- (2) step (b) is for about 2 minutes;
- (3) step (c) is effected immediately following step (b);
- (4) step (d) is effected about 2 minutes following step (c);
- (5) step (e) is effected immediately following step (d);
- (6) step (e) is for about 2 minutes; and
- (7) said pharmacological stress is adenosine or dipyridamole.

12. The method of claim 10, effected as described in Table 4.

13. A method of radioimaging a myocardial perfusion, the method comprising in sequence:

- (a) administering to a subject about 3 mCi Tl201 thallous chloride;
- (b) allowing said subject to rest;
- (c) radioimaging a heart of said subject;
- (d) subjecting said subject to a physical stress;
- (e) administering to said subject at a peak of said physical stress about 20-30 mCi Tc99m sestamibi; and
- (f) radioimaging said heart of said subject immediately following said peak stress, thereby radioimaging a myocardial perfusion.

14. The method of claim 13, comprising at least one or more of the following:

- (1) step (b) is for about 15 minutes;
- (2) step (c) is for about 2 minutes;
- (3) step (e) is effected about 30 - 60 minutes following step (d); and
- (4) step (f) is for about 2 minutes.

15. The method of claim 13, effected as described in Table 5.

16. A method of radioimaging a myocardial perfusion, the method comprising in sequence:

- (a) administering to a subject about 20-30 mCi Tc99m sestamibi;
- (b) allowing said subject to rest;
- (c) radioimaging a heart of said subject;
- (d) subjecting said subject to a physical stress;
- (e) administering to said subject at a peak of said physical stress about 3 mCi Tl201 thallous chloride;
- (f) radioimaging said heart of said subject; and
- (g) radioimaging said heart of said subject, thereby radioimaging a myocardial perfusion.

17. The method of claim 16, comprising at least one or more of the following:

- (1) step (b) is for about 15-30 minutes;
- (2) step (c) is for about 2 minutes;
- (3) step (d) is effected immediately following step (c);
- (4) step (f) is effected about 10-15 minutes following step (e);
- (5) step (f) is for about 4 minutes;
- (6) step (g) is effected about 4 hours following step (f); and
- (7) step (g) is for about 6 minutes.

18. The method of claim 16, effected as described in Table 6.

19. A method of radioimaging a myocardial perfusion, the method comprising in sequence:

- (a) administering to a subject about 3 mCi Tc99m sestamibi;
- (b) allowing said subject to rest;
- (c) radioimaging a heart of said subject;
- (d) subjecting said subject to a pharmacological stress;
- (e) administering to said subject at a peak of said pharmacological stress about 3 mCi Tl201 thallous chloride;
- (f) radioimaging said heart of said subject; and
- (g) radioimaging said heart of said subject, thereby radioimaging a myocardial perfusion.

20. The method of claim 19, comprising at least one or more of the following:

- (1) step (b) is for about 15-30 minutes;
- (2) step (c) is for about 2 minutes;
- (3) step (d) is effected immediately following step (c);
- (4) step (e) is effected about 2 minutes following step (d);
- (5) step (f) is effected immediately following step (e);
- (6) step (f) is for about 4 minutes;
- (7) step (g) is effected about 4 hours following step (f);
- (8) step (g) is for about 6 minutes; and
- (9) said pharmacological stress is adenosine or dipyridamole.

21. The method of claim 19, effected as described in Table 7.

22. A method of radioimaging a myocardial perfusion, the method comprising in sequence:

- (a) administering to a subject about 3 mCi Tc99m sestamibi;
- (b) radioimaging a heart of said subject;
- (c) subjecting said subject to a pharmacological stress;

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(d) administering to said subject at a peak of said pharmacological stress about 3 mCi Tl201 thallous chloride;

(e) radioimaging said heart of said subject; and

(f) radioimaging said heart of said subject, thereby radioimaging a myocardial perfusion.

23. The method of claim 22, comprising at least one or more of the following:

(1) step (b) is effected immediately following step (a);

(2) step (b) is for about 2 minutes;

(3) step (c) is effected immediately following step (b);

(4) step (d) is effected about 2 minutes following step (c);

(5) step (e) is effected immediately following step (d);

(6) step (e) is for about 4 minutes;

(7) step (f) is effected about 4 hours following step (e);

(8) step (f) is for about 6 minutes; and

(9) said pharmacological stress is adenosine or dipyridamole.

24. The method of claim 22, effected as described in Table 8.

25. A method of radioimaging a myocardial perfusion, the method comprising in sequence:

(a) administering to a subject about 3 mCi Tc99m sestamibi;

(b) allowing said subject to rest;

(c) radioimaging a heart of said subject;

(d) subjecting said subject to a pharmacological stress;

(e) administering to said subject at a peak of said pharmacological stress about 3 mCi Tl201 thallous chloride;

(f) allowing said subject to rest; and

(g) radioimaging said heart of said subject, thereby radioimaging a myocardial perfusion.

26. The method of claim 25, comprising at least one or more of the following:

- (1) step (b) is for about 30 minutes;
- (2) step (c) is for about 2 minutes;
- (3) step (d) is effected immediately following step (c);
- (4) step (e) is effected about 2 minutes following step (d);
- (5) step (f) is for about 2 minutes;
- (6) step (g) is effected immediately following step (f);
- (7) step (g) is for about four minutes; and
- (8) said pharmacological stress is adenosine or dipyridamole.

27. The method of claim 25, effected as described in Table 9.

28. A method of radioimaging a myocardial perfusion, the method comprising in sequence:

- (a) administering to a subject about 8-10 mCi Tc99m Teboroxime;
- (b) radioimaging a heart of said subject;
- (c) subjecting said subject to a pharmacological stress;
- (d) administering to said subject at a peak of said pharmacological stress about 20-30 mCi Tc99m Teboroxime; and
- (e) radioimaging said heart of said subject, thereby radioimaging a myocardial perfusion.

29. The method of claim 28, comprising at least one or more of the following:

- (1) step (b) is effected immediately following step (a);
- (2) step (b) is for about 2-10 minutes;
- (3) step (c) is effected immediately following step (b);
- (4) step (d) is effected about 2 minutes following step (c);
- (5) step (e) is effected immediately following or during step (d);
- (6) step (e) is for about 2-10 minutes; and
- (7) said pharmacological stress is adenosine or dipyridamole.

30. The method of claim 28, effected as described in Table 10.
31. A method of radioimaging a lung perfusion, the method comprising simultaneously:
- (a) administering to a subject less than about 5 mCi Tc99m Diethylene triamine-pentacetic acid (DTPA);
  - (b) administering to a subject less than about 5 mCi Tc99m MAA;
  - (c) radioimaging a lung of said subject, thereby radioimaging a lung perfusion.
32. The method of claim 31, comprising at least one or more of the following:
- (1) step (c) is for about 0-30 minutes; and
  - (2) said Tc99m Diethylene triamine-pentacetic acid is administered via a nebulizer.
33. The method of claim 31, effected as described in Table 11.
34. A method of radioimaging a bone inflammation or a bone cancer, the method comprising simultaneously:
- (a) administering to a subject about 20-30 mCi Tc99m MDP; and
  - (b) radioimaging a bone of said subject, thereby radioimaging a bone inflammation or a bone cancer.
35. The method of claim 34, comprising at least one or more of the following:
- (1) step (b) is effected about 0-60 minutes following step (a);
  - (2) step (b) is for about six minutes.
36. The method of claim 34, effected as described in Table 12.
37. A method of radioimaging an inflammatory process, the method comprising in sequence:



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- (a) administering to a subject about 2-3 mCi In 111 WBC; and
- (b) radioimaging said subject, thereby radioimaging an inflammatory process.

38. The method of claim 37, comprising at least one or more of the following:

- (1) step (b) is effected about 24 hours following step (a).
- (2) step (b) is for about 1 minute.

39. The method of claim 37, effected as described in Table 13.

40. A method of radioimaging a myocardial perfusion, the method comprising in sequence:

- (a) administering to a subject about 0.3 mCi Tl201 thallous chloride;
- (b) radioimaging a heart of said subject;
- (c) subjecting said subject to a physical stress;
- (d) administering to said subject at a peak of said physical stress about 3 mCi Tc99m sestamibi; and
- (e) radioimaging said heart of said subject, thereby radioimaging a myocardial perfusion.

41. The method of claim 40, comprising at least one or more of the following:

- (1) step (b) is effected about 10-15 minutes following step (a);
- (2) step (b) is for about 15 minutes;
- (3) step (c) is immediately following step (b);
- (4) step (e) is effected about 30-60 minutes following step (d); and
- (5) step (e) is for about 15 minutes.

42. The method of claim 40, effected as described in Table 14.

43. A method of radioimaging a myocardial perfusion, the method comprising in sequence:

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- (a) administering to a subject about 0.3 mCi Tc99m sestamibi;
- (b) radioimaging a heart of said subject;
- (c) subjecting said subject to a physical stress;
- (d) administering to said subject at a peak of said physical stress about 3 mCi Tc99m sestamibi; and
- (e) radioimaging said heart of said subject, thereby radioimaging a myocardial perfusion.

44. The method of claim 43, comprising at least one or more of the following:

- (1) step (b) is effected about 15-30 minutes following step (a);
- (2) step (b) is for about 15 minutes;
- (3) step (c) is effected immediately following step (b);
- (4) step (e) is effected about 30-60 minutes following step (d); and
- (5) step (e) is for about 15 minutes.

45. The method of claim 43, effected as described in Table 15.

46. A method of radioimaging a myocardial perfusion, the method comprising in sequence:

- (a) administering to a subject about 0.3 mCi Tl201 thallous chloride;
- (b) subjecting said subject to a physical stress;
- (c) administering to said subject at a peak of said physical stress about 3 mCi Tc99m sestamibi; and
- (d) radioimaging a heart of said subject, thereby radioimaging a myocardial perfusion.

47. The method of claim 46, comprising at least one or more of the following:

- (1) step (b) is effected immediately following step (a);
- (2) step (d) is effected about 30-60 minutes following step (c); and
- (3) step (d) is for about 5-15 minutes.

48. The method of claim 46, effected as described in Table 16.

49. A method of radioimaging a myocardial perfusion, the method comprising in sequence:

- (a) administering to a subject about 0.3 mCi Tl201 thallous chloride;
- (b) radioimaging a heart of said subject
- (c) subjecting said subject to a pharmacological stress;
- (d) administering to said subject at a peak of said pharmacological stress about 3 mCi Tc99m sestamibi; and
- (e) radioimaging said heart of said subject, thereby radioimaging a myocardial perfusion.

50. The method of claim 49, comprising at least one or more of the following:

- (1) step (b) is effected about 2 minutes following step (a);
- (2) step (b) is for about 15 minutes;
- (3) step (c) is effected immediately following step (b);
- (4) step (d) is effected about 2 minutes following step (c);
- (5) step (e) is effected immediately following step (d);
- (6) step (e) is for about 15 minutes; and
- (7) said pharmacological stress is adenosine or dipyridamole.

51. The method of claim 49, effected as described in Table 17.

52. A method of radioimaging a breast cancer, the method comprising in sequence:

- (a) administering to a subject about 0.3 mCi Tc99m sestamibi; and
- (b) radioimaging a breast of said subject, thereby radioimaging a breast cancer.

53. The method of claim 52, comprising at least one or more of the following:

- (1) step (b) is effected about 15-30 minutes following step (a);

- (2) step (b) is for about 15 minutes.

54. The method of claim 52, effected as described in Table 18.

55. A method of radioimaging a brain perfusion, the method comprising in sequence:

(a) simultaneously administering to a subject no more than about 3 mCi Tc99m exametazine (HMPAO), no more than about 3 mCi Tc99m ECD and no more than about 5 mCi I123 isofetamine hydrochloride; and

(b) radioimaging a brain of said subject, thereby radioimaging a brain perfusion.

56. The method of claim 55, comprising at least one or more of the following:

(1) step (b) is effected about 1 hour following step (a);

(2) step (b) is no more than 30 minutes.

57. The method of claim 55, effected as described in Table 19.

58. A method of radioimaging a brain perfusion, the method comprising in sequence:

(a) administering to a subject no more than about 3 mCi Tc99m exametazine (HMPAO); and

(b) radioimaging a brain of said subject, thereby radioimaging a brain perfusion.

59. The method of claim 58, comprising at least one or more of the following:

(1) step (b) is effected for no more than about 1 hour following step (a);

(2) step (b) is for no more than about 30 minutes.

60. The method of claim 58, effected as described in Table 20.

61. A method of radioimaging a brain perfusion, the method comprising in sequence:

- (a) administering to a subject no more than about 3 mCi Tc99m ECD; and
- (b) radioimaging a brain of said subject, thereby radioimaging a brain perfusion.

62. The method of claim 61, comprising at least one or more of the following:

- (1) step (b) is effected for no more than about 1 hour following step (a);
- (2) step (b) is for no more than about 30 minutes.

63. The method of claim 61, effected as described in Table 21.

64. A method of radioimaging a brain perfusion, the method comprising in sequence:

- (a) administering to a subject no more than about 5 mCi I 123 isofetamine hydrochloride; and
- (b) radioimaging a brain of said subject, thereby radioimaging a brain perfusion.

65. The method of claim 64, comprising at least one or more of the following:

- (1) step (b) is effected for no more than about 1 hour following step (a);
- (2) step (b) is for no more than about 30 minutes.

66. The method of claim 64, effected as described in Table 22.

67. A method of radioimaging a brain perfusion, the method comprising simultaneously:

- (a) administering to a subject no more than about 3 mCi Tc99m exametazine (HMPAO); and
- (b) radioimaging a brain of said subject, thereby radioimaging a brain perfusion.

68. The method of claim 67, wherein step (b) is for no more than 30 minutes.

69. The method of claim 67, effected as described in Table 23.

70. A method of radioimaging a brain perfusion, the method comprising simultaneously:

- (a) administering to a subject no more than about 3 mCi Tc99m ECD; and
- (b) radioimaging a brain of said subject, thereby radioimaging a brain perfusion.

71. The method of claim 70, wherein step (b) is for no more than about 30 minutes.

72. The method of claim 70, effected as described in Table 24.

73. A method of radioimaging a brain perfusion, the method comprising simultaneously:

- (a) administering to a subject no more than about 5 mCi I 123 isofetamine hydrochloride; and
- (b) radioimaging a brain of said subject, thereby radioimaging a brain perfusion.

74. The method of claim 73, wherein step (b) is for no more than about 30 minutes.

75. The method of claim 73, effected as described in Table 25.

76. A method of radioimaging a liver structure, the method comprising simultaneously:

- (a) administering to a subject about 0.5 mCi Tc99m mebrofenin; and



(b) radioimaging a liver of said subject, thereby radioimaging a liver structure.

77. The method of claim 76, wherein step (b) is for about 30 minutes.

78. The method of claim 76, effected as described in Table 26.

79. A method of radioimaging a lung perfusion, the method comprising simultaneously:

(a) administering to a subject no more than about 3 mCi of Tc99m DTPA and no more than 0.5 mCi of MAA or DTPA In 111; and

(b) radioimaging a lung of said subject, thereby radioimaging a lung perfusion.

80. The method of claim 79, wherein step (b) is for about 6 minutes.

81. The method of claim 79, effected as described in Table 27.

82. A method of radioimaging a myocardial perfusion (thallium rest), the method comprising simultaneously:

(a) radioimaging a heart of said subject; and

(b) administering to a subject about 4 mCi of Tl thallos chloride, thereby radioimaging a myocardial perfusion.

83. The method of claim 82, wherein step (a) is for about 2-20 minutes.

84. The method of claim 82, effected as described in Table 28.

85. A method of radioimaging a myocardial perfusion (thallium stress), the method comprising in sequence:

(a) subjecting a subject to a physical or pharmacological stress;

(b) administering to said subject at a peak of said physical stress about 4 mCi Tl201 thallos chloride; and

(c) radioimaging a heart of said subject, thereby radioimaging a myocardial perfusion.

86. The method of claim 85, comprising at least one or more of the following:

- (1) step (c) is effected immediately following step (b);
- (2) step (c) is for about 2-20 minutes; and
- (3) said pharmacological stress is adenosine or dipyridamole.

87. The method of claim 85, effected as described in Table 29.

88. A method of radioimaging a myocardial perfusion (teboroxime rest), the method comprising simultaneously:

- (a) radioimaging a heart of said subject; and
- (b) administering to a subject about 30 mCi of Tc99m teboroxime, thereby radioimaging a myocardial perfusion.

89. The method of claim 88, wherein step (a) is for about 15 minutes.

90. The method of claim 88, effected as described in Table 30.

91. A method of radioimaging a myocardial perfusion (teboroxime stress), the method comprising in sequence:

- (a) subjecting a subject to a physical or pharmacological stress;
- (b) administering to said subject at a peak of said physical stress about 4 mCi Tc99m Teboroxime; and
- (c) radioimaging a heart of said subject, thereby radioimaging a myocardial perfusion.

92. The method of claim 91, comprising at least one or more of the following:

- (1) step (c) is effected immediately following step (b);
- (2) step (c) is for about 2-20 minutes; and

- (3) said pharmacological stress is adenosine or dipyridamole.

93. The method of claim 91, effected as described in Table 31.

94. A method of radioimaging a myocardial perfusion (sestamibi rest), the method comprising simultaneously:

- (a) radioimaging a heart of said subject; and
- (b) administering to a subject about 30 mCi of Tc99m sestamibi, thereby radioimaging a myocardial perfusion.

95. The method of claim 94, wherein step (a) is for about 15 minutes.

96. The method of claim 94, effected as described in Table 32.

97. A method of radioimaging a myocardial perfusion (sestamibi stress), the method comprising in sequence:

- (a) subjecting a subject to a physical or pharmacological stress;
- (b) administering to said subject at a peak of said physical stress about 20-30 mCi of Tc99m sestamibi; and
- (c) radioimaging a heart of said subject, thereby radioimaging a myocardial perfusion.

98. The method of claim 97, comprising at least one or more of the following:

- (1) step (c) is effected immediately following step (b);
- (2) step (c) is for about 15 minutes; and
- (3) said pharmacological stress is adenosine or dipyridamole.

99. The method of claim 97, effected as described in Table 33.

100. A method of radioimaging a myocardial perfusion (tetrofosmin rest), the method comprising simultaneously:

- (a) radioimaging a heart of said subject; and

(b) administering to a subject about 30 mCi of Tc99m tetrofosmin, thereby radioimaging a myocardial perfusion.

101. The method of claim 100, wherein step (a) is for about 15 minutes.

102. The method of claim 100, effected as described in Table 34.

103. A method of radioimaging a myocardial perfusion (tetrofosmin stress), the method comprising in sequence:

- (a) subjecting a subject to a physical or pharmacological stress;
- (b) administering to said subject at a peak of said physical stress about 20-30 mCi of Tc99m tetrofosmin; and
- (c) radioimaging a heart of said subject, thereby radioimaging a myocardial perfusion.

104. The method of claim 103, comprising at least one or more of the following:

- (1) step (c) is effected immediately following or during step (b);
- (2) step (c) is for about 15 minutes; and
- (3) said pharmacological stress is adenosine or dipyridamole.

105. The method of claim 103, effected as described in Table 35.

106. A method of radioimaging a myocardial perfusion (Q12 rest), the method comprising simultaneously:

- (a) radioimaging a heart of said subject; and
- (b) administering to a subject about 30 mCi of Q12, thereby radioimaging a myocardial perfusion.

107. The method of claim 106, wherein step (a) is for about 15 minutes.

108. The method of claim 106, effected as described in Table 36.

109. A method of radioimaging a myocardial perfusion (Q12 stress), the method comprising in sequence:

- (a) subjecting a subject to a physical or pharmacological stress;
- (b) administering to said subject at a peak of said physical stress about 30 mCi of Q12; and
- (c) radioimaging a heart of said subject, thereby radioimaging a myocardial perfusion.

110. The method of claim 109, comprising at least one or more of the following:

- (1) step (c) is effected immediately following step (b);
- (2) step (c) is for about 15 minutes; and
- (3) said pharmacological stress is adenosine or dipyridamole.

111. The method of claim 109, effected as described in Table 37.

112. A method of radioimaging a myocardial perfusion (BMIPP-I123 rest), the method comprising simultaneously:

- (a) radioimaging a heart of said subject; and
- (b) administering to a subject about 5 mCi of BMIPP I-123, thereby radioimaging a myocardial perfusion.

113. The method of claim 112, wherein step (a) is for about 15 minutes.

114. The method of claim 112, effected as described in Table 38.

115. A method of radioimaging a myocardial perfusion (BMIPP I-123 stress), the method comprising in sequence:

- (a) subjecting a subject to a physical or pharmacological stress;
- (b) administering to said subject at a peak of said physical stress about 5 mCi of BMIPP I-123; and
- (c) radioimaging a heart of said subject, thereby radioimaging a myocardial perfusion.

116. The method of claim 115, comprising at least one or more of the following:

- (1) step (c) is effected immediately following step (b);
- (2) step (c) is for about 15 minutes; and
- (3) said pharmacological stress is adenosine or dipyridamole.

117. The method of claim 115, effected as described in Table 39.

118. A method of radioimaging a myocardial perfusion, the method comprising in sequence:

- (a) subjecting a subject to a physical or pharmacological stress;
- (b) administering to said subject at a peak of said physical stress about 30 mCi of a radiopharmaceutical; and
- (c) radioimaging a heart of said subject, thereby radioimaging a myocardial perfusion.

119. The method of claim 118, comprising at least one or more of the following:

- (1) step (c) is effected immediately following step (b);
- (2) step (c) is for about 10 minutes; and
- (3) said pharmacological stress is adenosine or dipyridamole.

120. The method of claim 118, effected as described in Table 40.

121. A method of radioimaging a myocardial perfusion, the method comprising simultaneously:

- (a) radioimaging a heart of a subject; and
- (b) administering to said subject about 30 mCi of a PET radiopharmaceutical, thereby radioimaging a myocardial perfusion.

122. The method of claim 121, comprising at least one or more of the following:



- (1) step (c) is effected immediately following step (b); and
- (2) step (c) is for about 10 minutes.

123. The method of claim 121, effected as described in Table 41.

124. A method of radioimaging a tumor, the method comprising simultaneously:

- (a) radioimaging a tumor of a subject; and
- (b) administering to said subject about 30 mCi of Tc99m Teboroxime, 30 mCi of Tc99m sestamibi, 30 mCi of Tc99m tetrofosmin or 4 mCi of Tl-201, thereby radioimaging a myocardial perfusion.

125. The method of claim 124, wherein step (a) is no more than about 5 minutes.

126. The method of claim 124, effected as described in Table 42.

127. A method of radioimaging a tumor, the method comprising simultaneously:

- (a) radioimaging a tumor of a subject; and
- (b) administering to said subject about 4 mCi of Tl201 thallous chloride and no more than about 30 mCi of Tc99m sestamibi, thereby radioimaging a tumor.

128. The method of claim 127, wherein step (a) is no more than about 5 minutes.

129. The method of claim 127, effected as described in Table 43.

130. A method of radioimaging a renal function, the method comprising simultaneously:

- (a) radioimaging a kidney of a subject; and
- (b) administering to said subject about 1 mCi of Tc99mDTPA and about 3-10 mCi of Tc99mMAG3, thereby radioimaging a renal function.

131. The method of claim 130, wherein step (a) is 10 minutes.
132. The method of claim 130, effected as described in Table 44.
133. A method of radioimaging a renal function, the method comprising simultaneously:
- (a) radioimaging a kidney of a subject; and
  - (b) administering to said subject about 1 mCi of Tc99m DTPA and about 1 mCi of Hippura nI-123, thereby radioimaging a renal function.
134. The method of claim 133, wherein step (a) is about 10 minutes.
135. The method of claim 133, effected as described in Table 45.
136. A method of radioimaging a brain perfusion, the method comprising simultaneously:
- (a) radioimaging a brain of a subject; and
  - (b) administering to said subject about 20 mCi of Tc99m ECD (neuro-lite) and about 20 mCi of HPMAO 99m labeled and about 5 mCi of Spectamint-123, thereby radioimaging a brain perfusion.
137. The method of claim 136, wherein step (a) is no more than about 30 minutes.
138. The method of claim 136, effected as described in Table 46.
139. A method of radioimaging a brain perfusion, the method comprising simultaneously:
- (a) radioimaging a brain of a subject; and
  - (b) administering to said subject no more than about 20 mCi of teboroxime, thereby radioimaging a brain perfusion.

140. The method of claim 139, wherein step (a) is no more than 30 minutes.
141. The method of claim 139, effected as described in Table 47.
142. A method of radioimaging a liver structure, the method comprising simultaneously:
- (a) radioimaging a liver of said subject; and
  - (b) administering to said subject no more than about 5 mCi of Tc99m sulfur colloid, thereby radioimaging a liver structure.
143. The method of claim 142, wherein step (a) is no more than 10 minutes.
144. The method of claim 142, effected as described in Table 48.
145. A method of radioimaging a liver function, the method comprising simultaneously:
- (a) radioimaging a liver of said subject; and
  - (b) administering to said subject no more than about 10 mCi of Tc99m disida, thereby radioimaging a liver structure.
146. The method of claim 145, wherein step (a) is effected every five minutes for up until 1 hour.
147. The method of claim 145, wherein the method further comprises administering an agent for gall bladder contraction 1 hour following step (b).
148. The method of claim 145, effected as described in Table 49.
149. A method of radioimaging a gastric emptying, the method comprising simultaneously:
- (a) radioimaging a stomach of a subject; and

(b) administering to said subject about 3 MBq of Tc99m Sulfur colloid or labeled solid food or 0.5 MBq In-111 DTPA labeled liquid food, thereby radioimaging a gastric emptying.

150. The method of claim 149, wherein step (a) is for a time until said stomach is empty of said labeled food.

151. The method of claim 149, effected as described in Table 50.

152. A method of radioimaging a cardiac vulnerable plaque, the method comprising in sequence:

(a) administering to a subject no more than about 5 mCi Tc99m annexin and no more than about 5mCi Tc99m AccuTec; and

(b) radioimaging a blood vessel of said subject, thereby radioimaging a cardiac vulnerable plaque.

153. The method of claim 152, comprising at least one or more of the following:

(1) step (b) is effected about 1 hour following step (a);

(2) step (b) is less than about 30 minutes.

154. The method of claim 152, effected as described in Table 51.

155. A method of radioimaging for prostate cancer, the method comprising in sequence:

(a) administering to a subject no more than about 5 mCi Prostatecint containing 111In capromed pendetide and

(b) radioimaging a prostate of said subject, thereby radioimaging for prostate cancer.

156. The method of claim 155, comprising at least one or more of the following:

(1) step (b) is effected about 24 - 72 hours following step (a);

- (2) step (b) is less than about 30 minutes.

157. The method of claim 155, effected as described in Table 52.

158. A method of radioimaging for SST receptor expressing tumors, the method comprising in sequence:

(a) administering to a subject no more than about 5 mCi Octreotide containing  $^{111}\text{In}$  DTPA; and

(b) radioimaging a body of said subject, thereby radioimaging for SST receptor expressing tumors.

159. The method of claim 158, comprising at least one or more of the following:

- (1) step (b) is effected about 24 hours following step (a);  
(2) step (b) is less than about 30 minutes.

160. The method of claim 158, effected as described in Table 53.

161. A method of radioimaging for neuroendocrine tumors, the method comprising in sequence:

(a) administering to a subject no more than about 20 mCi  $\text{Tc}^{99\text{m}}$  Neotec;  
and

(b) radioimaging a body of said subject, thereby radioimaging for neuroendocrine tumors.

162. The method of claim 161, comprising at least one or more of the following:

- (1) step (b) is effected about 1 hour following step (a);  
(2) step (b) is up to 30 minutes.

163. The method of claim 161, effected as described in Table 54.

164. A method of radioimaging for thrombii, the method comprising in sequence:

- (a) administering to a subject no more than about 20 mCi Tc99m Acutec;
- and
- (b) radioimaging blood vessels of said subject.

165. The method of claim 164, comprising at least one or more of the following:

- (1) step (b) is effected from about 0-20 minutes following step (a);
- (2) step (b) is less than about 30 minutes.

166. The method of claim 164, effected as described in Table 55.

167. A method of radioimaging a pheochromocytoma and/or myocardial failure, the method comprising in sequence:

- (a) administering to a subject no more than about 5 mCi I-123 iofetamine hydrochloride MIBG; and
- (b) radioimaging an adrenal gland or heart of said subject, thereby radioimaging a pheochromocytoma and/or myocardial failure.

168. The method of claim 167, comprising at least one or more of the following:

- (1) step (b) is effected about 24 hours following step (a);
- (2) step (b) is less than about 30 minutes.

169. The method of claim 167, effected as described in Table 56.

170. A method of radioimaging a cardiac stress, the method comprising in sequence:

- (a) administering to a subject about 4 mCi Tl201 thallous chloride;
- (b) radioimaging a heart of said subject;
- (c) subjecting said subject to a physical or pharmacological stress, wherein said pharmacological stress is at least one vasodilatory agent; and



(d) radioimaging a heart of said subject, thereby radioimaging a cardiac stress.

171. The method of claim 170, comprising at least one or more of the following:

- (1) step (b) is effected no more than about 2 minutes following step (a);
- (2) step (b) is for about 2-5 minutes;
- (3) step (c) is effected immediately following step (b);
- (4) step (d) is effected no more than about 5 minutes following step (c);
- (5) step (d) is for about 2-10 minutes; and
- (6) said at least one vasodilatory agent is adenosine or dipyridamole.

172. The method of claim 170, effected as described in Table 57.

173. A method of radioimaging a renal function, the method comprising in sequence:

- (a) administering to a subject about 2-4 mCi DTPA and/or Tc99mMAG3;
- (b) radioimaging a kidney of said subject;
- (c) subjecting said subject to a physical and/or at least one pharmacological stress; and
- (d) radioimaging a kidney of said subject.

174. The method of claim 173, comprising at least one or more of the following:

- (1) step (b) is for about 10-30 minutes;
- (2) step (c) is effected immediately following step (b);
- (3) step (d) is for about 10-30 minutes
- (4) said pharmacological stress is selected from the group consisting of captopril fuside, a vasodilatory agent and a diuretic agent.

175. The method of claim 173, effected as described in Table 58.

176. A method of radioimaging to determine Bexaar dosimetry, the method comprising simultaneously:

- (a) radioimaging a body of a subject; and
- (b) administering to said subject about 5 MCi/35 mg of I123 iofetamine hydrochloride, thereby radioimaging to determine Bexaar dosimetry.

177. The method of claim 176, wherein step (a) is for about 5 minutes.

178. The method of claim 176, effected as described in Table 59.

179. A method of radioimaging a parathyroid adenoma, the method comprising in sequence:

- (a) administering to a subject about 1 mCi thallium 201thallous chloride and about 15mCi Tc99m pertechnetate;
- (b) radioimaging a parathyroid of said subject, thereby radioimaging a parathyroid adenoma.

180. The method of claim 179, comprising at least one or more of the following:

- (1) step (b) is effected about 10 minutes following step (a); and
- (2) step (b) is for about 5 minutes.

181. The method of claim 179, effected as described in Table 60.

182. A method of radioimaging a parathyroid adenoma, the method comprising in sequence:

- (a) administering to a subject about 15 mCi Tc99m sestamibi and about 100 $\mu$ Ci I123;
- (b) radioimaging a parathyroid of said subject, thereby radioimaging a parathyroid adenoma.

183. The method of claim 182, comprising at least one or more of the following:

- (1) step (b) is effected about 10 minutes following step (a); and
- (2) step (b) is for about 5 minutes.

184. The method of claim 182, effected as described in Table 61.

185. A method of radioimaging a thyroid cancer, the method comprising in sequence:

- (a) administering to a subject about 10 mCi Tc99m MDP and about 4 mCi I-131;
- (b) radioimaging a thyroid of said subject, thereby radioimaging a thyroid cancer.

186. The method of claim 185, comprising at least one or more of the following:

- (1) step (b) is effected about 2 hours following step (a); and
- (2) step (b) is for about 30 minutes.

187. The method of claim 185, effected as described in Table 62.

188. A method of radioimaging an endocrine tumor, the method comprising in sequence:

- (a) administering to a subject about 15 mCi Tc99m MDP and about 4 mCi In111 octeotride;
- (b) radioimaging a body of said subject, thereby radioimaging an endocrine tumor.

189. The method of claim 188, comprising at least one or more of the following:

- (1) step (b) is effected no more than about 2 hours following step (a); and
- (2) step (b) is for about 30 minutes.

190. The method of claim 188, effected as described in Table 63.

191. A method of radioimaging an endocrine tumor, the method comprising in sequence:

- (a) administering to a subject about 4 mCi  $^{111}\text{In}$  octeotride;
- (b) administering to a subject about 15 mCi  $^{99\text{m}}\text{Tc}$  MDP;
- (c) radioimaging a body of said subject, thereby radioimaging an endocrine tumor.

192. The method of claim 191, comprising at least one or more of the following:

- (1) step (b) is effected no more than about 3 days following step (a);
- (2) step (c) is effected no more than about 2 hours following step (b); and
- (3) step (c) is for about 30 minutes.

193. The method of claim 191, effected as described in Table 64.

194. A method of radioimaging a prostate tumor, the method comprising in sequence:

- (a) administering to a subject about 3 mCi  $^{111}\text{In}$  capromab pentitide;
- (b) administering to a subject about 15 mCi  $^{99\text{m}}\text{Tc}$  RBCs;
- (c) radioimaging a pelvis or abdomen of said subject, thereby radioimaging a prostate tumor.

195. The method of claim 194, comprising at least one or more of the following:

- (1) step (b) is effected no more than about 3 days following step (a);
- (2) step (c) is effected no more than about 2 hours following step (b); and
- (3) step (c) is for about 30 minutes.

196. The method of claim 194, effected as described in Table 65.

197. A method of radioimaging a bone infection, the method comprising in sequence:

- (a) administering to a subject about 3 mCi  $^{111}\text{In}$  WBC;

- (b) administering to a subject about 15 mCi Tc99m colloid;
- (c) radioimaging a bone of said subject, thereby radioimaging a bone infection.

198. The method of claim 197, comprising at least one or more of the following:

- (1) step (b) is effected no more than 3 days following step (a);
- (2) step (c) is effected no more than 2 hours following step (b); and
- (3) step (c) is for about 30 minutes.

199. The method of claim 197, effected as described in Table 66.

200. A method of radioimaging a neck or head cancer invasion of a bone or cartilage, the method comprising in sequence:

- (a) administering to a subject about 2 mCi Tl201 thallous chloride and about 15 mCi Tc99m MDP;
- (b) radioimaging a bone or cartilage of said subject, thereby radioimaging a neck or head cancer invasion of a bone or cartilage.

201. The method of claim 200, comprising at least one or more of the following:

- (1) step (b) is effected about 2 hours following step (a); and
- (2) step (b) is for about 30 minutes.

202. The method of claim 200, effected as described in Table 67.

203. A method of radioimaging a pathological condition, the method comprising in sequence:

- (a) administering to a subject about 2 mCi In111WBCs;
- (b) administering to said subject about 1 mCi Tl201 thallous chloride and about 10 mCi Tc99m sestamibi; and
- (c) radioimaging a body of said subject, thereby radioimaging a pathological condition.

204. The method of claim 203, comprising at least one or more of the following:

- (1) step (b) is effected about 2 days following step (a); and
- (2) step (c) is for about 30 minutes;
- (3) the pathological condition is selected from the group consisting of an infection, a tumor and a myocardial perfusion.

205. The method of claim 203, effected as described in Table 68.

206. A method of radioimaging a myocardial ischemia, the method comprising in sequence:

- (a) administering to a subject about 2 mCi I123 BMIPP;
- (b) administering to said subject about 1 mCi Tl201 thallous chloride and about 10 mCi of a Tc99m labeled chemical selected from the group consisting of sestamibi and teboroxime; and
- (c) radioimaging a heart of said subject, thereby radioimaging a myocardial ischemia.

207. The method of claim 206, comprising at least one or more of the following:

- (1) step (b) is effected about 48 hours following step (a); and
- (2) step (c) is for about 30 minutes;
- (3) step (c) is effected immediately following step (b).

208. The method of claim 206, effected as described in Table 69.

209. A method of radioimaging a pathological condition or a fever of unknown origin, the method comprising in sequence:

- (a) administering to a subject about 2 mCi In111WBC;
- (b) administering to said subject about 15 mCi 99m Fanoselomab; and
- (c) radioimaging a body of said subject, thereby radioimaging a pathological condition or fever of unknown origin.



210. The method of claim 209, comprising at least one or more of the following:

- (1) step (b) is effected about 24 hours following step (a); and
- (2) step (c) is for about 30 minutes.
- (3) step (c) is effected immediately following step (b).

211. The method of claim 209, effected as described in Table 70.

212. A method of radioimaging to indicate schizophrenia or Parkinson's disease, the method comprising in sequence:

- (a) administering to a subject about 2 mCi I123 IBZM;
- (b) administering to said subject about 15 mCi Tc99m HMPAO; and
- (c) radioimaging a brain of said subject, thereby radioimaging to indicate schizophrenia or Parkinson's disease.

213. The method of claim 212, comprising at least one or more of the following:

- (1) step (b) is effected about 24 hours following step (a); and
- (2) step (c) is for about 30 minutes.
- (3) step (c) is effected immediately following step (b).

214. The method of claim 212, effected as described in Table 71.

215. A method of radioimaging a tumor, a tumor perfusion and/or for differentiating a tumor from infection, the method comprising in sequence:

- (a) administering to a subject about 2 mCi In111 WBC;
- (b) administering to said subject Tc99m sestamibi, Tc99m Arcitumo Mab and Tl201 thallous chloride; and
- (c) radioimaging an organ and/or body of said subject, thereby radioimaging a tumor.

216. The method of claim 215, comprising at least one or more of the following:

- (1) step (b) is effected about 24 hours following step (a);
- (2) step (c) is for about 30 minutes;
- (3) step (c) is effected about 5 minutes following step (b);
- (4) a dose of Tc99m sestamibi and Tc99m Arcitumo Mab is each about 10 mCi; and
- (5) a dose of Tl201 thallous chloride is about 1 mCi.

217. The method of claim 215, effected as described in Table 72.

218. A method of radioimaging a renal function, the method comprising in sequence:

- (a) administering to a subject about 2 mCi In111 DTPA;
- (b) administering to said subject about 15 mCi Tc99m MAG3; and
- (c) radioimaging a kidney of said subject, thereby radioimaging a renal function.

219. The method of claim 218, comprising at least one or more of the following:

- (1) step (b) is effected about 24 hours following step (a);
- (2) step (c) is for about 30 minutes;
- (3) step (c) is effected about 5 minutes following step (b);

220. The method of claim 218, effected as described in Table 73.

221. A method of radioimaging a tumor perfusion, the method comprising in sequence:

- (a) administering to a subject about 1 mCi Tl thallous chloride;
- (b) administering to said subject about 15 mCi Tc99m teboroxime or about 15 mCi Tc99m sestamibi; and
- (c) radioimaging an organ of said subject, thereby radioimaging a tumor perfusion.

222. The method of claim 221, comprising at least one or more of the following:

- (1) step (b) is effected simultaneously with step (a);
- (2) step (c) is for about 30 minutes;
- (3) step (c) is effected immediately following step (b).

223. The method of claim 221, effected as described in Table 74.

224. A method of radioimaging a myocardial perfusion and an apoptosis in a blood vessel plaque, the method comprising in sequence:

- (a) administering to a subject about 1 mCi Tlthallous chloride;
- (b) administering to said subject about 15 mCi Tc99m Annexin; and
- (c) radioimaging a heart and blood vessels of said subject, thereby radioimaging a myocardial perfusion and apoptosis in a blood vessel plaque.

225. The method of claim 224, comprising at least one or more of the following:

- (1) step (b) is effected simultaneously with step (a);
- (2) step (c) is for about 30 minutes;
- (3) step (c) is effected less than about 1 hour following step (b);

226. The method of claim 224, effected as described in Table 75.

227. A method of radioimaging to differentiate between infection and bone marrow activation, the method comprising in sequence:

- (a) administering to a subject about 2 mCi In111WBC;
- (b) administering to said subject about 15 mCi Tc99m sulfur colloid; and
- (c) radioimaging a body of said subject, thereby radioimaging a tumor perfusion.

228. The method of claim 227, comprising at least one or more of the following:

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- (1) step (b) is effected about 24 hours following step (a);
- (2) step (c) is for about 30 minutes;
- (3) step (c) is effected immediately following step (b);

229. The method of claim 227, effected as described in Table 76.

230. A method of radioimaging an osteomyelitis, the method comprising in sequence:

- (a) administering to a subject about 2 mCi  $^{111}\text{In}$  WBC;
- (b) administering to said subject about 15 mCi  $^{99\text{m}}\text{Tc}$  MDP; and
- (c) radioimaging a bone of said subject, thereby radioimaging an osteomyelitis.

231. The method of claim 230, comprising at least one or more of the following:

- (1) step (b) is effected about 24 hours following step (a);
- (2) step (c) is for about 30 minutes;
- (3) step (c) is effected immediately following step (b).

232. The method of claim 230, effected as described in Table 77.

233. A method of radioimaging an inflammation, the method comprising in sequence:

- (a) administering to a subject about 5 mCi Gallium 67;
- (b) administering to said subject about 15 mCi  $^{111}\text{In}$  WBCs; and
- (c) radioimaging a body of said subject, thereby radioimaging an inflammation.

234. The method of claim 233, comprising at least one or more of the following:

- (1) step (b) is effected simultaneously with step (a);
- (2) step (c) is for about 30 minutes; and
- (3) step (c) is effected about 72 hours following step (b).

235. The method of claim 233, effected as described in Table 78.

236. A method of radioimaging a myocardial perfusion and apoptosis in a blood vessel plaque, the method comprising in sequence:

- (a) administering to a subject about 2 mCi  $^{111}\text{In}$  annexin;
- (b) administering to said subject about 15 mCi  $^{99\text{m}}\text{Tc}$  teboroxime or about 2 mCi  $^{201}\text{Tl}$  thallous chloride; and
- (c) radioimaging a heart of said subject, thereby radioimaging a myocardial perfusion and apoptosis in a blood vessel plaque.

237. The method of claim 236, comprising at least one or more of the following:

- (1) step (b) is effected about 24 hours following step (a);
- (2) step (c) is for about 30 minutes;
- (3) step (c) is effected no more than about 3 minutes following step (b).

238. The method of claim 236, effected as described in Table 79.

239. A method of radioimaging a myocardial perfusion, the method comprising in sequence:

- (a) administering to a subject about 2 mCi  $^{201}\text{Tl}$  thallous chloride;
- (b) administering to said subject about 15 mCi  $^{99\text{m}}\text{Tc}$  pyrophosphate; and
- (c) radioimaging a heart of said subject, thereby radioimaging a myocardial perfusion.

240. The method of claim 239, comprising at least one or more of the following:

- (1) step (b) is effected simultaneously with step (a);
- (2) step (c) is for about 30 minutes; and
- (3) step (c) is effected about 1 hour following step (b).

241. The method of claim 239, effected as described in Table 80.

242. A method of radioimaging a myocardial perfusion, the method comprising simultaneously:

- (a) radioimaging a heart of said subject; and
- (b) administering to a subject about 15 mCi of Tc99m pyrophosphate and about 2 mCi of Tl 201 thallous chloride, thereby radioimaging a myocardial perfusion.

243. The method of claim 242, wherein step (a) is for about 30 minutes.

244. The method of claim 242, effected as described in Table 81.

245. A method of radioimaging a myocardial perfusion or cardiac vulnerable plaque, the method comprising simultaneously:

- (a) administering to a subject about 5 mCi In111 annexin;
- (b) administering to said subject about 5 mCi Tc99m Accutec;
- (c) subjecting said subject to a pharmacological stress;
- (d) administering to said subject about 1 mCi Tl201 thallous chloride; and
- (e) radioimaging a heart and blood vessels of said subject, thereby radioimaging a myocardial perfusion or cardiac vulnerable plaque.

246. The method of claim 245, comprising at least one or more of the following:

- (1) step (b) is effected about 24 hours following step (a);
- (2) step (c) is effected immediately following step (b);
- (3) said pharmacological stress is adenosine or dipyridamole;
- (4) step (d) is effected about 2 minutes following step (c);
- (5) step (e) is for about 30 minutes.

247. The method of claim 245, effected as described in Table 82.

248. A method of radioimaging a glucose metabolism, the method comprising simultaneously:



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- (a) administering to a subject about 30-50mCi FDG; and
- (b) radioimaging a body of said subject, thereby radioimaging a glucose metabolism.

249. The method of claim 248, comprising at least one or more of the following:

- (1) step (b) is effected immediately following step (a); and
- (2) step (b) is for less than about 30 minutes.

250. The method of claim 248, effected as described in Table 83.

251. The method of any of the preceding claims, wherein said imaging is effected using a camera which comprises:

- (i) at least one radioactive-emission detector designed and constructed to image radioactive emission from the said tissue or body;
- (ii) a position-tracking device communicating with said at least one radioactive-emission detector and configured to provide positional information for said at least one radioactive-emission; and
- (iii) a data processor, designed and configured for receiving data inputs from said position tracking device and said at least one radioactive-emission detector, and for generating an image of the tissue or body.

252. A method of packaging a radiopharmaceutical selected from the group consisting of Tl201 thallous chloride, Tc99m sestamibi, Tc 99m Teboroxime, Tc 99m DTPA, MAA, Tc 99m MDP, In 111 WBC, Tc 99m exametazine (HMPAO), Tc 99m ECD, I 123 isofetamine hydrochloride, I 123 isofetamine hydrochloride, Tc 99m mebrofenin, DTPA In 111, tetrofosmin, Tc 99m MAG3, Hippuran I-123, neuro-lite, Tc 99m sulfur colloid, Tc 99m disida, Tc99m Annexin, Tc99m AccuTec, Proscint containing 111 In DTPA, Octreotide containing 111 In DTPA, Tc 99m neotec, MIBG containing I 123 iofetamine hydrochloride, Tc 99m pertechnetate, I 123, Tc 99m MDP, In 111 capromab pentitide, Tc 99m RBC, I 123 BMIPP, Tc 99m Fanoselomab, I 123 IBZM, Tc 99m ArcitumoMab, Gallium 67, Tc 99m pyrophosphate, In 111 annexin, F-18-Fluorodeoxyglucose (FDG), F-18-Fluoromisonidazole, F-18-3'-

Fluoro-3'-deoxythymidine (FLT), F-18-Fluoromethyl choline (FCH), F-18-4-Fluoro-m-tyrosine (FMT), F-18-6-Fluoro-L-DOPA, F-18-FP- $\beta$ -CIT, F-18-Pencyclovir (FHBG), F-18-Fuoroestradiol (FES), C-11-Methionine, Tc-99m-P280, Acutect®, C-11-Raclopride, I-123-iodobenzamide (IBZM), C-11-carfentanil, C-11- $\alpha$ -methyl-L-tryptophan, C-11-5-Hydroxytryptophan, F-18-MPPF, F-18-Altanserin, C-11-Acetate, C-11-Palmitate and F-18-Fluorodopamine, the method comprising packaging said radiopharmaceutical in a package and providing in association with the package in printed and/or electronic form instruction of use according to any of the methods of the preceding claims.

253. An article of manufacturing produced according to the method of claim 252.

254. A diagnostic pharmaceutical kit comprising a packaged dose unit of a diagnostic radiopharmaceutical having a dose equivalent of 2.5 mrem or less per kg body weight.

255. The diagnostic pharmaceutical kit of claim 254, wherein said packaged dose unit has a dose equivalent of 2 mrem or less per kg body weight.

256. The diagnostic pharmaceutical kit of claim 254, wherein said packaged dose unit has a dose equivalent of 1 mrem or less per kg body weight.

257. A diagnostic pharmaceutical kit comprising a packaged dose unit of diagnostic radiopharmaceutical having a dose equivalent of 150 mrem or less.

258. The diagnostic pharmaceutical kit of any of claims 254-257, wherein said diagnostic radiopharmaceutical is a radiotracer.

259. The diagnostic pharmaceutical kit of claim 258, wherein a radioisotope and a recognition binding moiety of said radiotracer are packaged in individual containers.

260. The diagnostic pharmaceutical kit of claim 254, wherein a purity of a radioisotope of said diagnostic radiopharmaceutical is at least 60 %.

261. The diagnostic pharmaceutical kit of claim 254, wherein a purity of a radioisotope of said diagnostic radiopharmaceutical is at least 90 %.

262. The diagnostic pharmaceutical kit of claim 254, wherein said diagnostic radiopharmaceutical is  $^{13}\text{N}$ -Ammonia and whereas said packaged dose unit comprises 0.01-5 mCi.

263. The diagnostic pharmaceutical kit of claim 254, wherein said diagnostic radiopharmaceutical is  $^{18}\text{F}$ -Fludeoxyglucose and whereas said packaged dose unit comprises 0.1-3 mCi.

264. The diagnostic pharmaceutical kit of claim 254, wherein said diagnostic radiopharmaceutical is  $^{18}\text{F}$ -Sodium Fluoride and whereas said packaged dose unit comprises 0.1-3 mCi.

265. The diagnostic pharmaceutical kit of claim 254, wherein said diagnostic radiopharmaceutical is  $^{81\text{m}}\text{Kr}$ -Krypton and whereas said packaged dose unit comprises 0.05-2 mCi.

266. The diagnostic pharmaceutical kit of claim 254, wherein said diagnostic radiopharmaceutical is  $^{111}\text{In}$ -Indium Capromab pendetide and whereas said packaged dose unit comprises 0.01-2 mCi.

267. The diagnostic pharmaceutical kit of claim 254, wherein said diagnostic radiopharmaceutical is  $^{99\text{m}}\text{Tc}$ -Technetium Arcitumomab and whereas said packaged dose unit comprises 0.05-5 mCi.

268. The diagnostic pharmaceutical kit of claim 254, wherein said diagnostic radiopharmaceutical is  $^{111}\text{In}$ -Indium Pentetreotide and whereas said packaged dose unit comprises 0.005-1 mCi.

269. The diagnostic pharmaceutical kit of claim 254, wherein said diagnostic radiopharmaceutical is  $^{125}\text{I}$ -Iodide Albumin and whereas said packaged dose unit comprises 0.0005-0.005 mCi.

270. The diagnostic pharmaceutical kit of claim 254, wherein said diagnostic radiopharmaceutical is  $^{51}\text{Cr}$ -Sodium Chromate and whereas said packaged dose unit comprises 0.001-0.05 mCi.

271. The diagnostic pharmaceutical kit of claim 254, wherein said diagnostic radiopharmaceutical is  $^{99\text{m}}\text{Tc}$ -Technetium Disofenin and whereas said packaged dose unit comprises 0.005-1 mCi.

272. The diagnostic pharmaceutical kit of claim 254, wherein said diagnostic radiopharmaceutical is  $^{99\text{m}}\text{Tc}$ -Technetium Sestamibi and whereas said packaged dose unit comprises 0.01-5 mCi.

273. A composition of matter comprising a low dose of at least one radiopharmaceutical intended for administration in whole to a human subject of a particular age and/or weight.

274. The composition of matter of claim 273, wherein said low dose is a dose below the maximal dose allowable to be administered to said human subject of said particular age and/or weight.

275. The composition of matter of claim 274, wherein said maximal dose is the lower of 5 REM and a dose that following administration and distribution in a body of the subject does not accumulate in any specific organ in said body in excess of 15 Rads.

276. The composition of matter of any of claims 273 to 275, wherein said radiopharmaceutical is selected from the group consisting of [18F]Fluorodeoxyglucose (FDG), [18F]-Fluoromisonidazole, [18F]3'-Fluoro-3'-

deoxythymidine (FLT), [18F]Fluoromethyl choline (FCH), [18F]4-Fluoro-m-tyrosine (FMT), [18F]6-Fluoro-L-DOPA, [18F]FP- $\beta$ CIT, [18F]Pencyclovir (FHBG), [18F]Fuoroestradiol (FES), [11C]Methionine,  $^{111}\text{In}$ -Pentetreotide,  $^{99\text{m}}\text{Tc}$ -P829,  $^{99\text{m}}\text{Tc}$ -P280,  $^{123}\text{I}$ -VIP (vasoactive intestinal peptide),  $^{131}\text{I}$ -NP-59, [11C]Raclopride,  $^{123}\text{I}$ -IBZM, [11C]Carfentanil, [11C] $\alpha$ -methyl-L-tryptophan, [11C]5-Hydroxytryptophan, [18F]MPPF, [18F]Altanserin, [11C]Acetate, [11C]Palmitate, [18F]Fluorodopamine,  $^3\text{H}$ -water,  $^3\text{H}$ -inulin,  $^{11}\text{C}$ -carbonmonoxide,  $^{13}\text{N}$ -ammonia,  $^{14}\text{C}$ -inulin,  $^{15}\text{O}$ - $\text{H}_2\text{O}$ ,  $^{15}\text{O}$ - $\text{O}_2$ ,  $^{18}\text{F}$ -fluorodeoxyglucose,  $^{18}\text{F}$ -sodium fluoride,  $^{51}\text{Cr}$ -erythrocytes (RBC),  $^{57}\text{Co}$ -vitamin  $\text{B}_{12}$  (cyanocobalamin),  $^{58}\text{Co}$ -vitamin  $\text{B}_{12}$  (cyanocobalamin),  $^{59}\text{Fe}$ -citrate,  $^{60}\text{Co}$ -vitamin  $\text{B}_{12}$  (cyanocobalamin),  $^{67}\text{Ga}$ -citrate,  $^{68}\text{Ga}$ -citrate,  $^{75}\text{Se}$ -selenomethionine,  $^{81\text{m}}\text{Kr}$ -krypton for inhalation, oral administration or injections,  $^{82}\text{Rb}$ ,  $^{85}\text{Sr}$ -nitrate,  $^{90}\text{Y}/^{111}\text{In}$ -ibritumomab tiuxetan ( $^{90}\text{Y}/^{111}\text{In}$ -Zevalin),  $^{99\text{m}}\text{Tc}$ -albumin microspheres,  $^{99\text{m}}\text{Tc}$ -disofenin, lidofenin and mebrofenin,  $^{99\text{m}}\text{Tc}$ -DMSA,  $^{99\text{m}}\text{Tc}$ -DTPA (injection),  $^{99\text{m}}\text{Tc}$ -DTPA (aerosol),  $^{99\text{m}}\text{Tc}$ -ECD (ethylene cystate dimer),  $^{99\text{m}}\text{Tc}$ -exametazime (HMPAO),  $^{99\text{m}}\text{Tc}$ -glucoheptonate,  $^{99\text{m}}\text{Tc}$ -HEDP,  $^{99\text{m}}\text{Tc}$ -HMDP,  $^{99\text{m}}\text{Tc}$ -HSA,  $^{99\text{m}}\text{Tc}$ -MAA,  $^{99\text{m}}\text{Tc}$ -MAG<sub>3</sub>,  $^{99\text{m}}\text{Tc}$ -MDP,  $^{99\text{m}}\text{Tc}$ -tetrofosmin,  $^{99\text{m}}\text{Tc}$ -sestamibi,  $^{99\text{m}}\text{Tc}$ -oral administrations,  $^{99\text{m}}\text{Tc}$ -pertechnetate,  $^{99\text{m}}\text{Tc}$ -pyrophosphate,  $^{99\text{m}}\text{Tc}$ -RBC *in vitro* and *in vivo* labeling,  $^{99\text{m}}\text{Tc}$ -sulfur colloid,  $^{99\text{m}}\text{Tc}$ -teboroxime,  $^{99\text{m}}\text{Tc}$ -white blood cells,  $^{111}\text{In}$ -ibritumomab tiuxetan ( $^{111}\text{In}$ -Zevalin),  $^{111}\text{In}$ -DTPA,  $^{111}\text{In}$ -platelets,  $^{111}\text{In}$ -RBC,  $^{111}\text{In}$ -white blood cells,  $^{123}\text{I}$ -hippuran,  $^{123}\text{I}$ -IMP,  $^{123}\text{I}$ -mIBG,  $^{123}\text{I}$ -sodium iodide,  $^{124}\text{I}$ -sodium iodide,  $^{125}\text{I}$ -fibrinogen,  $^{125}\text{I}$ -IMP,  $^{125}\text{I}$ -mIBG,  $^{125}\text{I}$ -sodium iodide,  $^{126}\text{I}$ -sodium iodide,  $^{130}\text{I}$ -sodium iodide,  $^{131}\text{I}$ -hippuran,  $^{131}\text{I}$ -HSA,  $^{131}\text{I}$ -MAA,  $^{131}\text{I}$ -mIBG,  $^{131}\text{I}$ -Rose Bengal,  $^{131}\text{I}$ -sodium iodide,  $^{127}\text{Xe}$ -inhalation and injection,  $^{133}\text{Xe}$ -inhalation and injection,  $^{197}\text{Hg}$ -chlormerodrin,  $^{198}\text{Au}$ -colloid and  $^{201}\text{Tl}$ -chloride, Cu-62, Ga-68, Indium-111 Capromab pendetide, Indium In-111 Satumomab Pendetide, Technetium Tc 99m Arcitumomab (CEA-Scan), Technetium Tc 99m Fanolesomab, Technetium Tc 99m Nofetumomab Merpentan, Indium In 111 Oxyquinoline, Indium In 111 Pentetate, Indium In 111 Pentetreotide, Iobenguane, Radioiodinated, IofetamineI 123, Iothalamate Sodium I 125, Iodide 125 Albumin, Radioiodinated Albumin, SodiumChromate Cr 51, (Sodium) Pertechnetate Tc 99m, Technetium Tc 99m Depreotide, Technetium Tc 99m Apcitide, TechnetiumTc 99m Bicisate, Technetium Tc 99m Disofenin (HIDA), Chromic Phosphate, SR 89 Chloride (Metastron), Technetium Tc 99m Oxidronate, Technetium Tc 99m (Pyro-

and trimeta-) Phosphates, Technetium Tc 99m Sulfur Colloid, Technetium Tc 99m HDP, Technetium Tc 99m Sulphur colloid and radiopharmaceuticals which comprise an isotope selected from the group consisting of  $^{198}\text{Au}$ ,  $^{11}\text{C}$ ,  $^{14}\text{C}$ ,  $^{51}\text{Cr}$ ,  $^{57}\text{Co}$ ,  $^{58}\text{Co}$ ,  $^{60}\text{Co}$ ,  $^{62}\text{Cu}$ ,  $^{18}\text{F}$ ,  $^{59}\text{Fe}$ ,  $^{67}\text{Ga}$ ,  $^{68}\text{Ga}$ ,  $^3\text{H}$ ,  $^{153}\text{Sm}$ ,  $^{197}\text{Hg}$ ,  $^{111}\text{I}$ ,  $^{123}\text{I}$ ,  $^{124}\text{I}$ ,  $^{125}\text{I}$ ,  $^{126}\text{I}$ ,  $^{130}\text{I}$ ,  $^{131}\text{I}$ ,  $^{133}\text{I}$ ,  $^{111}\text{In}$ ,  $^{81}\text{Kr}$ ,  $^{127}\text{Xe}$ ,  $^{133}\text{Xe}$ ,  $^{67}\text{Cu}$ ,  $^{177}\text{Lu}$ ,  $^{13}\text{N}$ ,  $^{15}\text{O}$ ,  $^{82}\text{Rb}$ ,  $^{117\text{m}}\text{Sn}$ ,  $^{85}\text{Sr}$ ,  $^{89}\text{Sr}$ ,  $^{52}\text{Fe}$ ,  $^{113\text{m}}\text{In}$ ,  $^{99\text{m}}\text{Tc}$ ,  $^{201}\text{Tl}$ .

277. The composition of matter of any of claims 274 to 276, wherein said low dose is selected from the group consisting of:

- (i) less than 90 % of said maximal dose;
- (ii) less than 85 % of said maximal dose;
- (iii) less than 80 % of said maximal dose;
- (iv) less than 75 % of said maximal dose;
- (v) less than 70 % of said maximal dose;
- (vi) less than 65 % of said maximal dose;
- (vii) less than 60 % of said maximal dose;
- (viii) less than 55 % of said maximal dose;
- (ix) less than 50 % of said maximal dose;
- (x) less than 45 % of said maximal dose;
- (xi) less than 40 % of said maximal dose;
- (xii) less than 35 % of said maximal dose;
- (xiii) less than 30 % of said maximal dose;
- (xiv) less than 25 % of said maximal dose;
- (xv) less than 20 % of said maximal dose;
- (xvi) less than 15 % of said maximal dose;
- (xvii) less than 10 % of said maximal dose;
- (xviii) less than 9 % of said maximal dose;
- (xix) less than 8 % of said maximal dose;
- (xx) less than 7 % of said maximal dose;
- (xxi) less than 6 % of said maximal dose;
- (xxii) less than 5 % of said maximal dose;
- (xxiii) less than 4 % of said maximal dose;
- (xxiv) less than 3 % of said maximal dose;

- (xxv) less than 2 % of said maximal dose;
- (xxvi) less than 1 % of said maximal dose;
- (xxvii) less than 0.9 % of said maximal dose;
- (xxviii) less than 0.8 % of said maximal dose;
- (xxix) less than 0.7 % of said maximal dose;
- (xxx) less than 0.6 % of said maximal dose;
- (xxxi) less than 0.5 % of said maximal dose;
- (xxxii) less than 0.4 % of said maximal dose;
- (xxxiii) less than 0.3 % of said maximal dose;
- (xxxiv) less than 0.2 % of said maximal dose;
- (xxxv) less than 0.1 % of said maximal dose;
- (xxxvi) less than 0.05 % of said maximal dose; or
- (xxxvii) less than 0.01 % of said maximal dose;

278. A method of radioimaging a region of interest in a subject, the method comprising:

- (a) administering to the subject the composition of matter of any of claims 273 to 277; and
- (b) using a high sensitivity radioactive-emission camera for collecting radioactive-emission data from the subject, thereby radioimaging the region of interest in the subject.

279. The method of claim 278, wherein said high sensitivity is selected from the group consisting of:

- (a) sensitivity in terms of speed of data collection and spatial resolution, at least as good as a gold standard for PET imaging for at rest myocardial perfusion with N-13-ammonia ( $\text{NH}_3$ ), at a dose of 740 MBq with attenuation correction;
- (b) sensitivity sufficient for reconstructing an image under a Cobalt wire Nema test of a line source of 5 mCi cobalt with a line spread function of less than 7 mm Full Width Half Maximum (FWHM) through air at a distance of at least 100 mm;
- (c) sensitivity sufficient for resolving through air at a distance of at least 100 mm under a Nema Bar Phantom test of gaps formed between 1 mm wide led bars positioned less than 7 mm apart from one another over a uniform cobalt disc;



(d) sensitivity operative for image acquisition of a full organ in less than 10 seconds at a spatial resolution, capable of identifying objects not greater than about 7 mm X 7 mm X 7 mm with a signal-to-noise ratio of at least 4 to 1 or better; and/or

(e) sensitivity allowing acquisition of at least 1 out of every 5000 emitted photons while allowing a reconstruction of a 3D image with a resolution of not more than 5 mm and energy resolution of not more than 15 %.

280. The method of claim 278, wherein said sensitivity is selected from the group consisting of:

at least 2 fold that of said gold standard for PET imaging;

at least 3 fold that of said gold standard for PET imaging;

at least 4 fold that of said gold standard for PET imaging;

at least 5 fold that of said gold standard for PET imaging;

at least 6 fold that of said gold standard for PET imaging;

at least 7 fold that of said gold standard for PET imaging;

at least 8 fold that of said gold standard for PET imaging;

at least 9 fold that of said gold standard for PET imaging;

at least 10 fold that of said gold standard for PET imaging;

at least 20 fold that of said gold standard for PET imaging;

at least 30 fold that of said gold standard for PET imaging;

at least 50 fold that of said gold standard for PET imaging;

at least 100 fold that of said gold standard for PET imaging;

sufficient for reconstructing an image under a Cobalt wire Nema test of said line source of 5 mCi cobalt with a line spread function of less than 6 mm Full Width Half Maximum (FWHM) through air at said distance of at least 100 mm;

sufficient for reconstructing an image under a Cobalt wire Nema test of said line source of 5 mCi cobalt with a line spread function of less than 5 mm Full Width Half Maximum (FWHM) through air at said distance of at least 100 mm;

sufficient for reconstructing an image under a Cobalt wire Nema test of said line source of 5 mCi cobalt with a line spread function of less than 4 mm Full Width Half Maximum (FWHM) through air at said distance of at least 100 mm;

sufficient for reconstructing an image under a Cobalt wire Nema test of said line source of 5 mCi cobalt with a line spread function of less than 3 mm Full Width Half Maximum (FWHM) through air at said distance of at least 100 mm;

sufficient for reconstructing an image under a Cobalt wire Nema test of said line source of 5 mCi cobalt with a line spread function of less than 2 mm Full Width Half Maximum (FWHM) through air at said distance of at least 100 mm;

sufficient for reconstructing an image under a Cobalt wire Nema test of said line source of 5 mCi cobalt with a line spread function of about 1 mm Full Width Half Maximum (FWHM) through air at said distance of at least 100 mm;

sufficient for resolving through air at said distance of at least 100 mm under said Nema Bar Phantom test of said gaps formed between said 1 mm wide led bars positioned less than 6 mm apart from one another over said uniform cobalt disc;

sufficient for resolving through air at said distance of at least 100 mm under said Nema Bar Phantom test of said gaps formed between said 1 mm wide led bars positioned less than 5 mm apart from one another over said uniform cobalt disc;

sufficient for resolving through air at said distance of at least 100 mm under said Nema Bar Phantom test of said gaps formed between said 1 mm wide led bars positioned less than 4 mm apart from one another over said uniform cobalt disc;

sufficient for resolving through air at said distance of at least 100 mm under said Nema Bar Phantom test of said gaps formed between said 1 mm wide led bars positioned less than 3 mm apart from one another over said uniform cobalt disc;

sufficient for resolving through air at said distance of at least 100 mm under said Nema Bar Phantom test of said gaps formed between said 1 mm wide led bars positioned less than 2 mm apart from one another over said uniform cobalt disc;

sufficient for resolving through air at said distance of at least 100 mm under said Nema Bar Phantom test of said gaps formed between said 1 mm wide led bars positioned less than 1 mm apart from one another over said uniform cobalt disc;

sufficient for resolving through air at said distance of at least 100 mm under said Nema Bar Phantom test of said gaps formed between said 1 mm wide led bars positioned less than 0.5 mm apart from one another over said uniform cobalt disc;

sufficient for resolving through air at said distance of at least 100 mm under said Nema Bar Phantom test of said gaps formed between said 1 mm wide led bars positioned less than 0.1 mm apart from one another over said uniform cobalt disc;

operative for image acquisition of said full organ in less than 10 seconds at said spatial resolution, capable of identifying objects not greater than about 6 mm X 6 mm X 6 mm with said signal-to-noise ratio of at least 4 to 1 or better;

operative for image acquisition of said full organ in less than 10 seconds at said spatial resolution, capable of identifying objects not greater than about 5 mm X 5 mm X 5 mm with said signal-to-noise ratio of at least 4 to 1 or better;

operative for image acquisition of said full organ in less than 10 seconds at said spatial resolution, capable of identifying objects not greater than about 4 mm X 4 mm X 4 mm with said signal-to-noise ratio of at least 4 to 1 or better;

operative for image acquisition of said full organ in less than 10 seconds at said spatial resolution, capable of identifying objects not greater than about 3 mm X 3 mm X 3 mm with said signal-to-noise ratio of at least 4 to 1 or better;

operative for image acquisition of said full organ in less than 10 seconds at said spatial resolution, capable of identifying objects not greater than about 2 mm X 2 mm X 2 mm with said signal-to-noise ratio of at least 4 to 1 or better;

operative for image acquisition of said full organ in less than 10 seconds at said spatial resolution, capable of identifying objects not greater than about 1 mm X 1 mm X 1 mm with said signal-to-noise ratio of at least 4 to 1 or better;

operative for image acquisition of said full organ in less than 10 seconds at said spatial resolution, capable of identifying objects not greater than about 0.5 mm X 0.5 mm X 0.5 mm with said signal-to-noise ratio of at least 4 to 1 or better; and/or

operative for image acquisition of said full organ in less than 10 seconds at said spatial resolution, capable of identifying objects not greater than about 0.1 mm X 0.1 mm X 0.1 mm with said signal-to-noise ratio of at least 4 to 1 or better.

281. A method of packaging the composition-of matter of any of claims 273 to 277, the method comprising placing said low dose of said at least one radiopharmaceutical intended for said administration in whole to said human subject of said particular age and/or weight in a container or a syringe.

282. A method of manufacturing the composition-of matter of any of claims 273 to 277, the method comprising generating said at least one radiopharmaceutical

collecting said at least one radiopharmaceutical at a time needed for having said low dose.

283. A method of radioimaging comprising:

(a) administering to a human subject a low dose of a first radiopharmaceutical; and

(b) acquiring data representing a distribution of said first radiopharmaceutical in at least a section of the body of said subject during at least one time window.

284. A method of radioimaging comprising:

(a) administering to a human subject a low dose of a first radiopharmaceutical; and

(b) acquiring data representing a distribution of said first radiopharmaceutical in at least a section of the body of said subject during at least one short time window.

285. The method of claims 283 or 284, wherein said section of a body comprises the heart.

286. The method of claim 285, further comprising:

(c) subjecting said human subject to stress following said administering of said first radiopharmaceutical; and

(d) administering to said human subject a dose of at least a second radiopharmaceutical, prior to acquiring said data.

287. The method of claim 286, further comprising acquiring from said subject data representing a distribution of said first radiopharmaceutical in said subject during at least one short time window prior to subjecting said human subject to said stress.

288. The method of claim 286, wherein said first radiopharmaceutical comprises thallium-201 at a dose of about 3 mCi.

289. The method of claim 286, wherein said first radiopharmaceutical comprises technetium-99m-methoxyisobutylisonitrile (sestamibi).

290. The method of any of claims 288 to 289, wherein said second radiopharmaceutical comprises technetium-99m-methoxyisobutylisonitrile (sestamibi) at a dose of from about 20 to about 30 mCi.

291. The method of claim 289, wherein said second radiopharmaceutical comprises thallium-201 at a dose of about 3 mCi.

292. The method of claim 290, said first radiopharmaceutical comprises technetium-99m-methoxyisobutylisonitrile (sestamibi) at a dose of from about 8 to about 10 mCi.

293. The method of claim 291, said first radiopharmaceutical comprises technetium-99m-methoxyisobutylisonitrile (sestamibi) at a dose of about 3 mCi.

294. The method of any of claims 292 to 293, wherein said short time window is not greater than about 6 minutes.

295. The method of claim 290, wherein said first radiopharmaceutical comprises thallium-201 at a dose of about 3 mCi and said short window time is not greater than about 4 minutes.

296. The method of claim 287, wherein said first radiopharmaceutical comprises thallium-201 at a dose of about 3 mCi, said second radiopharmaceutical comprises technetium-99m-methoxyisobutylisonitrile (sestamibi) at a dose of from about 20 to about 30 mCi and said short time window is not greater than about 4 minutes.

297. The method of claim 296, wherein said data representing a distribution of said first radiopharmaceutical in said subject is acquired during a short time window of up to about 2 minutes.

298. The method of claim 297, wherein said data representing a distribution of said second radiopharmaceutical in said subject is acquired during a short time window of up to about 2 minutes.

299. The method of claim 298, wherein a time period of from about 10 to about 15 minutes is allowed to elapse between said administering of said first radiopharmaceutical and said acquiring of data representing a distribution of said first pharmaceutical.

300. The method of claim 299, wherein a time period from about 30 to about 60 minutes is allowed to elapse between said administering of said second radiopharmaceutical and said acquiring of data representing a distribution of said second pharmaceutical.

301. The method of claim 298, wherein a time period of from about 2 minutes is allowed to elapse between said administering of said first radiopharmaceutical and said acquiring of data representing a distribution of said first pharmaceutical.

302. The method of claim 301, said acquiring of data representing a distribution of said second pharmaceutical is performed immediately following administering of said second radiopharmaceutical.

303. The method of claim 300, wherein said stress comprises exercise stress.

304. The method of claim 302, wherein said stress comprises pharmacological stress.

305. The method of claim 287, wherein said first radiopharmaceutical comprises technetium-99m- methoxyisobutylisonitrile (sestamibi) at a dose of from about 8 to about 10 mCi, said second radiopharmaceutical comprises technetium-99m- methoxyisobutylisonitrile (sestamibi) at a dose of from about 20 to about 30 mCi and said short time window is not greater than about 4 minutes.

306. The method of claim 305, wherein said data representing a distribution of said first radiopharmaceutical in said subject is acquired during a short time window of up to about 2 minutes.

307. The method of claim 306, wherein said data representing a distribution of said second radiopharmaceutical in said subject is acquired during a short time window of up to about 2 minutes.

308. The method of claim 307, wherein a time period of about 30 minutes is allowed to elapse between said administering of said first radiopharmaceutical and said acquiring of data representing a distribution of said first pharmaceutical.

309. The method of claim 308, wherein a time period from about 30 to about 60 minutes is allowed to elapse between said administering of said second radiopharmaceutical and said acquiring of data representing a distribution of said second pharmaceutical.

310. The method of claim 309, wherein said stress comprises exercise stress.

311. The method of claim 307, wherein said acquiring of data representing a distribution of said first pharmaceutical is performed immediately following administering of said first radiopharmaceutical.

312. The method of claim 311, wherein said acquiring of data representing a distribution of said second pharmaceutical is performed immediately following administering of said second radiopharmaceutical.



313. The method of claim 312, wherein said stress comprises pharmacological stress.

314. The method of claim 287, wherein said first radiopharmaceutical comprises technetium-99m- methoxyisobutylisonitrile (sestamibi) at a dose of about 3 mCi, said second radiopharmaceutical comprises thallium-201 at a dose of about 3 mCi, and said short time window is not greater than about 6 minutes.

315. The method of claim 314, wherein said data representing a distribution of said first radiopharmaceutical in said subject is acquired during a short time window of up to about 2 minutes.

316. The method of claim 315, wherein said data representing a distribution of said second radiopharmaceutical in said subject is acquired during a short time window of up to about 4 minutes.

317. The method of claim 316, wherein a time period of about 30 minutes is allowed to elapse between said administering of said first radiopharmaceutical and said acquiring of data representing a distribution of said first pharmaceutical.

318. The method of claim 317, wherein a time period from about 10 to about 15 minutes is allowed to elapse between said administering of said second radiopharmaceutical and said acquiring of data representing a distribution of said second pharmaceutical.

319. The method of claim 318, wherein said stress comprises exercise stress.

320. The method of claim 317, wherein said acquiring of data representing a distribution of said second pharmaceutical is performed immediately following administering of said second radiopharmaceutical.

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321. The method of claim 320, wherein said stress comprises pharmacological stress.

322. The method of claim 316, wherein said acquiring of data representing a distribution of said first pharmaceutical is performed immediately following administering of said first radiopharmaceutical.

323. The method of claim 322, wherein said acquiring of data representing a distribution of said second pharmaceutical is performed immediately following administering of said second radiopharmaceutical.

324. The method of claim 323, wherein said stress comprises pharmacological stress.

325. The method of claim 286, wherein said first radiopharmaceutical comprises thallium-201 at a dose of about 3 mCi, said second radiopharmaceutical comprises technetium-99m- methoxyisobutylisonitrile (sestamibi) at a dose of from about 20 to about 30 mCi, and said short time window is not greater than about 2 minutes.

326. The method of claim 325, wherein said acquiring of data representing a distribution of said first radiopharmaceutical and said acquiring of data representing a distribution of second radiopharmaceutical are performed simultaneously.

327. The method of claim 325, wherein a time period of from about 30 to about 60 minutes is allowed to elapse between said administering of said second radiopharmaceutical and said acquiring of data representing a distribution of said first and said second radiopharmaceuticals.

328. The method of claim 327, wherein said stress comprises exercise stress.

329. The method of claim 286, wherein said first radiopharmaceutical comprises technetium-99m-methoxyisobutylisonitrile (sestamibi) at a dose of about 3 mCi, said second radiopharmaceutical comprises thallium-201 at a dose of about 3 mCi, and said short time window is not greater than about 4 minutes.

330. The method of claim 329, wherein said acquiring of data representing a distribution of said first radiopharmaceutical and said acquiring of data representing a distribution of second radiopharmaceutical are performed simultaneously.

331. The method of claim 330, wherein a time period of from about 2 minutes is allowed to elapse between said administering of said second radiopharmaceutical and said acquiring of data representing a distribution of said first and said second radiopharmaceuticals.

332. The method of any of claims 283 to 284, wherein said section of a body comprises the lung.

333. The method of claim 332, wherein said first radiopharmaceutical comprises a combination of Tc-99m-diethylene triamine pentaacetate (DTPA), Tc-99m-macro-aggregated albumin, and iodine-123.

334. The method of claim 333, wherein a concentration of said Tc-99m-macro-aggregated albumin is up to about 5 mCi.

335. The method of claim 334, wherein said acquiring of data is performed immediately following administering of said first radiopharmaceutical.

336. The method of any of claims 283 to 284, wherein said section of a body comprises the bones.

337. The method of claim 332, wherein said first radiopharmaceutical comprises Tc-99m-disodium dihydrogen methylenediphosphate at a dose of from about 20 to about 30 mCi.

338. The method of claim 337, wherein a time period of up to about 60 minutes is allowed to elapse between said administering of said radiopharmaceutical and said acquiring of data, and wherein , wherein said acquiring of data is performed at an energy window of from about 3 to about 15 percent.

339. The method of claim 287, wherein said first radiopharmaceutical comprises technetium-99m-teboroxime at a dose of from about 8 to about 10 mCi, said second radiopharmaceutical comprises technetium-99m- teboroxime at a dose of from about 20 to about 30 mCi and said short time window is not greater than about 4 minutes.

340. The method of claim 339, wherein said data representing a distribution of said first radiopharmaceutical in said subject is acquired during a short time window of up to about 2 minutes.

341. The method of claim 340, wherein said data representing a distribution of said second radiopharmaceutical in said subject is acquired during a short time window of up to about 2 minutes.

342. The method of claim 341, wherein said acquiring of data representing a distribution of said first pharmaceutical is performed immediately following administering of said first radiopharmaceutical.

343. The method of claim 342, wherein a time period of about 10 minutes is allowed to elapse between said acquiring of data representing a distribution of said first pharmaceutical and said subjecting to said stress.

344. The method of claim 343, wherein said acquiring of data representing a distribution of said second pharmaceutical is performed immediately following administering of said second radiopharmaceutical.

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345. The method of claim 344, wherein said stress comprises pharmacological stress.

346. The method of any of claims 283 or 284, wherein said section of a body comprises the heart.

347. The method of claim 346, further comprising:

(c) subjecting said human subject to stress following said administering of said first radiopharmaceutical; and

(d) administering to said human subject a low dose of at least a second radiopharmaceutical, prior to acquiring said data.

348. The method of claim 347, further comprising acquiring from said subject data representing a distribution of said first radiopharmaceutical in said subject during at least one time window prior to subjecting said human subject to said stress.

349. The method of claim 348, wherein said first radiopharmaceutical comprises thallium-201 at a dose of about 0.3 mCi.

350. The method of claim 348, wherein said first radiopharmaceutical comprises technetium-99m- methoxyisobutylisonitrile (sestamibi) at a dose about 0.3 mCi.

351. The method of any of claims 349 to 350, wherein said second radiopharmaceutical comprises technetium-99m- methoxyisobutylisonitrile (sestamibi) at a dose about 3 mCi.

352. The method of claim 348, wherein said second radiopharmaceutical comprises technetium-99m- methoxyisobutylisonitrile (sestamibi) at a dose about 30 mCi.

353. The method of claim 351, wherein said data representing a distribution of said first radiopharmaceutical in said subject is acquired during a time window of about 15 minutes.

354. The method of claim 353, wherein said data representing a distribution of said second radiopharmaceutical in said subject is acquired during a time window of about 15 minutes.

355. The method of claim 353, wherein said first radiopharmaceutical comprises thallium-201 at a dose of about 0.3 mCi, and wherein said data representing a distribution of said second radiopharmaceutical in said subject is acquired during a time window of about 2 minutes.

356. The method of claim 354, wherein a time period from about 30 to about 60 minutes is allowed to elapse between said administering of said second radiopharmaceutical and said acquiring of data representing a distribution of said second pharmaceutical.

357. The method of claim 356, wherein said first radiopharmaceutical comprises thallium-201 at a dose of about 0.3 mCi, and wherein a time period from about 10 to about 15 minutes is allowed to elapse between said administering of said thallium-201 and said acquiring of data representing a distribution of said thallium-201.

358. The method of claim 356, wherein said first radiopharmaceutical comprises technetium-99m- methoxyisobutylisonitrile (sestamibi) at a dose about 0.3 mCi, and wherein a time period from about 30 minutes is allowed to elapse between said administering of technetium-99m- methoxyisobutylisonitrile (sestamibi) and said acquiring of data representing a distribution of technetium-99m- methoxyisobutylisonitrile (sestamibi).

359. The method of any of claims 357 to 358, wherein said stress comprises exercise stress.

360. The method of claim 355, wherein said first radiopharmaceutical comprises thallium-201 at a dose of about 0.3 mCi, and wherein a time period of about 2 minutes is allowed to elapse between said administering of said thallium-201 and said acquiring of data representing a distribution of said thallium-201.

361. The method of claim 354, wherein said first radiopharmaceutical comprises technetium-99m- methoxyisobutylisonitrile (sestamibi) at a dose about 0.3 mCi, and wherein said acquiring of data representing a distribution of said first radiopharmaceutical is performed immediately following administering of said first radiopharmaceutical.

362. The method of any of claims 360 to 361, wherein said acquiring of data representing a distribution of said second radiopharmaceutical is performed immediately following administering of said second radiopharmaceutical.

363. The method of claim 362, wherein said stress comprises pharmacological stress.

364. The method of claim 347, wherein said first radiopharmaceutical comprises thallium-201 at a dose of about 0.3 mCi, said second radiopharmaceutical comprises technetium-99m- methoxyisobutylisonitrile (sestamibi) at a dose of from about 3 to about 5 mCi, and wherein said acquiring of data representing a distribution of said thallium-201 and said technetium-99m- methoxyisobutylisonitrile (sestamibi) is performed simultaneously.

365. The method of claim 364, wherein said data representing a distribution of said thallium-201 and said technetium-99m- methoxyisobutylisonitrile (sestamibi) in said subject is acquired during a time window of from about 5 to about 15 minutes.

366. The method of claim 365, wherein a time period of from about 30 to about 60 minutes is allowed to elapse between said administering of technetium-99m- methoxyisobutylisonitrile (sestamibi) and said acquiring of data representing a



distribution of said thallium-201 and said technetium-99m- methoxyisobutylisonitrile (sestamibi).

367. The method of any of claims 347 to 366, wherein said acquiring of data is performed at an energy window of from about 3 to about 15 percent.

368. The method of any of claims 283 to 284, wherein said first radiopharmaceutical comprises thallium-201 at a dose of up to about 4 mCi, and said time window is from about 2 to about 20 minutes.

369. The method of any of claims 283 to 284, wherein said first radiopharmaceutical is selected from the group consisting of Tc-99m-teboroxime, Tc-99m- methoxyisobutylisonitrile (sestamibi), Tc-99m-tetrofosmin, Tc-99m-furifosmin (Q12), and Tc-99m-beta-methyl-p-iodophenylpentadecanoic acid (BMIPP).

370. The method of claim 369, wherein a dose of said first radiopharmaceutical is up to about 30 mCi, and said time window is up to about 15 minutes.

371. The method of any of claims 369 to 370, wherein said subject is subjected to stress prior to acquiring of said data.

372. The method of any of claims 367 to 371 applied to cardiac perfusion studies.

373. The method of claim 369, wherein said first radiopharmaceutical is Tc-99m- methoxyisobutylisonitrile (sestamibi), applied to tumor imaging.

374. The method of any of claims 283 to 284, wherein said radiopharmaceutical is a combination of thallium-201 at a dose of up to 4 mCi and Tc-99m- methoxyisobutylisonitrile (sestamibi) at a dose of up to about 30 mCi, applied to tumor imaging.

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375. The method of any of claims 283 to 284, wherein said radiopharmaceutical is a combination of In-111-diethylene triamine pentaacetate (DTPA) at a dose of 0.2 mCi and Tc-99m-mercaptoacetyltriglycine (MAG3) at a dose of up to about 10 mCi, and said section of the body is the kidney.

376. The method of any of claims 283 to 284, wherein said radiopharmaceutical is a combination of In-111-diethylene triamine pentaacetate (DTPA) at a dose of from about 0.3 to about 1 mCi and I-123-iodohippurate sodium (hippuran) at a dose of up to about 10 mCi, and said section of the body is the kidney.

377. The method of any of claims 283 to 284, wherein said radiopharmaceutical is Tc-99m at a dose of up to about 5 mCi, applied to brain perfusion mapping.

378. The method of any of claims 283 to 284, wherein said radiopharmaceutical is a combination of Tc-99m-Exametazine (HMPAO) at a dose of up to about 20 mCi, Tc-99m N,N'(1,2-ethlenediyl)bis-L-cysteine diethyl ester (Tc-99m ECD) at a dose of up to about 20 mCi, and I-123 iofetamine hydrochloride, at a dose of up to about 5 mCi, applied to brain perfusion mapping.

379. The method of any of claims 283 to 284, wherein said radiopharmaceutical is a combination of

Tc-99m-diisopropyl iminodiacetic acid (disulfenine), Tc-99m-2,2'-[[2-[(3-bromo-2,4,6-trimethylphenyl)-amino]-2-oxoethyl] imino] bisacetic acid (Tc-99m-mebrofenin), and Tc-99m-dimethyl iminodiacetic acid (HIDA), applied to liver function study.

380. The method of any of claims 378 to 379, wherein said data is acquired immediately following administering of said first radiopharmaceutical at an energy window of from about 3 to about 15 percent.

381. The method of any of claims 379 to 380, applied to dynamic process imaging.

382. The method of any of claims 283 to 331 and 338 to 372, applied to the study of ventricular function study.

383. The method of any of claims 283 to 284, wherein said first radiopharmaceutical comprises a combination of Tc-99m-colloid and In-111-diethylene triamine pentaacetate (DTPA), applied to the study of dual phase gastric emptying.

384. A method of radioimaging comprising:

(a) administering to a human subject a dose of the composition of any of claims 349 to 351; and

(b) acquiring data representing a distribution of each of said radiopharmaceutical of said composition in at least a section of the body of said subject.

385. A composition comprising a first radiopharmaceutical and a second radiopharmaceutical being different from the first radiopharmaceutical, provided that if said first radiopharmaceutical is Tc-99m said second radiopharmaceutical is not Thallium 201 and vice versa.

386. The composition of claim 385, wherein both said first and said second radiopharmaceuticals are at low doses.

387. A composition comprising a low dose of a first radiopharmaceutical and a low dose of a second radiopharmaceutical being different from the first radiopharmaceutical.

388. A kit comprising at least two compositions for generating at least two radiopharmaceuticals, wherein said at least two radiopharmaceuticals are:

Tl-201-thallous chloride; and

Tc-99m-pertechnetate.

389. The kit of claim 388, wherein a dose of said Tl-201-thallous chloride is up to about 1 mCi and a dose of said Tc-99m-pertechnetate is up to about 15 mCi.

390. A kit comprising at least two compositions for generating at least two radiopharmaceuticals, wherein said at least two radiopharmaceuticals are:

Tc-99m- methoxyisobutylisonitrile (sestamibi); and  
I-123.

391. The kit of claim 390, wherein a dose of said Tc-99m-methoxyisobutylisonitrile (sestamibi) is about 15 mCi and a dose of said I-123 is up to about 100  $\mu$ Ci.

392. A kit comprising at least two compositions for generating at least two radiopharmaceuticals, wherein said at least two radiopharmaceuticals are:

I-123; and

Tc-99m- red blood cells or Tc-99m-dihydrogen methylenediphosphate (medronate).

393. The kit of claim 392, wherein a dose of said I-123 is about 4 mCi, a dose of said Tc-99m- red blood cells is up to about 10 mCi and a dose of said Tc-99m-dihydrogen methylenediphosphate (medronate) is up to about 10 mCi.

394. A kit comprising at least two compositions for generating at least two radiopharmaceuticals, wherein said at least two radiopharmaceuticals are:

In-111-L-Cysteinamide, D-phenylalanyl-L-cysteinyl-L-phenylalanyl-D-tryptophyl-L-lysyl-L-threonyl-N-[2-hydroxy-1-(hydroxy-methyl) propyl]-, cyclic 7)-disulfide (In-111-octreotide); and

Tc-99m-dihydrogen methylenediphosphate (medronate).

395. The kit of claim 394, wherein a dose of said In-111-octreotide is up to about 3 mCi and a dose of said Tc-99m- medronate is up to about 15 mCi.

396. A kit comprising at least two compositions for generating at least two radiopharmaceuticals, wherein said at least two radiopharmaceuticals are:

In-111-capromab pendetide; and  
Tc-99m-red blood cells.

397. The kit of claim 396, wherein a dose of said In-111-capromab pendetide is of up to about 2 mCi and a dose of said Tc-99m-red blood cells is up to about 15 mCi.

398. A kit comprising at least two compositions for generating at least two radiopharmaceuticals, wherein said at least two radiopharmaceuticals are:

Tc-99m-colloid; and  
In-111-white blood cells.

399. The kit of claim 398, wherein a dose of said Tc-99m-colloid is up to about 15 mCi and a dose of said In-111-white blood cells is up to about 3 mCi.

400. A kit comprising at least two compositions for generating at least two radiopharmaceuticals, wherein said at least two radiopharmaceuticals are:

Tl-201-thallous chloride; and  
Tc-99m-dihydrogen methylenediphosphate (medronate).

401. The kit of claim 400, wherein a dose of said Tl-201-thallous chloride is up to about 2 mCi and a dose of said Tc-99m-dihydrogen methylenediphosphate (medronate) is up to about 15 mCi.

402. A kit comprising at least two compositions for generating at least two radiopharmaceuticals, wherein said at least two radiopharmaceuticals are:

Tl-201-thallous chloride;  
Tc-99m-methoxyisobutylisonitrile (sestamibi); and  
In-111-white blood cells.

403. The kit of claim 402, wherein a dose of said Tl-201-thallous chloride is up to about 1 mCi, a dose of said Tc-99m-methoxyisobutylisonitrile (sestamibi) is up to about 10 mCi, and a dose of said In-111-white blood cells is up to about 2 mCi.

404. A kit comprising at least two compositions for generating at least two radiopharmaceuticals, wherein said at least two radiopharmaceuticals are:

Tl-201-thallous chloride;  
dihydrogen methylenediphosphate (medronate); and  
In-111-white blood cells.

405. The kit of claim 404, wherein a dose of said Tl-201-thallous chloride is up to about 1 mCi, a dose of said dihydrogen methylenediphosphate (medronate) is up to about 10 mCi, and a dose of said In-111-white blood cells is up to about 2 mCi.

406. A kit comprising at least two compositions for generating at least two radiopharmaceuticals, wherein said at least two radiopharmaceuticals are:

Tl-201-thallous chloride;  
Tc-99m-teboroxime or Tc-99m-methoxyisobutylisonitrile (sestamibi); and  
I-123-beta-methyl-p-iodophenylpentadecanoic acid (BMIPP).

407. The kit of claim 406, wherein a dose of said Tl-201-thallous chloride is up to about 1 mCi, a dose of said Tc-99m-teboroxime or Tc-99m-methoxyisobutylisonitrile (sestamibi) is up to 10 mCi, and a dose of said I-123-beta-methyl-p-iodophenylpentadecanoic acid (BMIPP) is up to about 2 mCi.

408. A kit comprising at least two compositions for generating at least two radiopharmaceuticals, wherein said at least two radiopharmaceuticals are:

Tc-99m-Fanositelomab; and  
In-111-white blood cells.

409. The kit of claim 408, wherein a dose of said Tc-99m-Fanositelomab is up to about 15 mCi and a dose of said In-111-white blood cells is up to about 2 mCi.

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410. A kit comprising at least two compositions for generating at least two radiopharmaceuticals, wherein said at least two radiopharmaceuticals are:

I-123-iodobenzamide (IBZM); and

Tc-99m-Exametazine (HMPAO).

411. The kit of claim 410, wherein a dose of said I-123-iodobenzamide (IBZM) is up to about 2 mCi and a dose of said Tc-99m-Exametazine (HMPAO) is about 15 mCi.

412. A kit comprising at least two compositions for generating at least two radiopharmaceuticals, wherein said at least two radiopharmaceuticals are:

In-111-labeled antibody;

Tc-99m- methoxyisobutylisonitrile (sestamibi) or Tc-99m- Arcitumomab;

and

Tl-201-thallous chloride.

413. The kit of claim 412, wherein a dose of said In-111-labeled antibody is up to about 1 mCi, a dose of said Tc-99m- methoxyisobutylisonitrile (sestamibi) or Tc-99m-Arcitumomab is up to about 10 mCi and a dose of said Tl-201-thallous chloride is up to about 1 mCi.

414. A kit comprising at least two compositions for generating at least two radiopharmaceuticals, wherein said at least two radiopharmaceuticals are:

In-111-diethylene triamine pentaacetate (DTPA); and

Tc-99m-mercaptoacetyltriglycine (MAG3).

415. The kit of claim 414, wherein a dose of said In-111-diethylene triamine pentaacetate (DTPA) is up to about 2 mCi and a dose of said Tc-99m-mercaptoacetyltriglycine (MAG3) is up to about 15 mCi.

416. A kit comprising at least two compositions for generating at least two radiopharmaceuticals, wherein said at least two radiopharmaceuticals are:

Tl-201-thallous chloride; and



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Tc-99m-teboroxime or Tc-99m-methoxyisobutylisonitrile (sestamibi).

417. The kit of claim 416, wherein a dose of said Tl-201-thallous chloride is up to about 1 mCi and a dose of said Tc-99m-teboroxime or Tc-99m-methoxyisobutylisonitrile (sestamibi) is up to about 15 mCi.

418. A kit comprising at least two compositions for generating at least two radiopharmaceuticals, wherein said at least two radiopharmaceuticals are:

Tc-99m-sulfur colloid; and  
In-111-white blood cells.

419. The kit of claim 418, wherein a dose of said Tc-99m-sulfur colloid is up to about 15 mCi and a dose of said In-111-white blood cells is up to about 2 mCi.

420. A kit comprising at least two compositions for generating at least two radiopharmaceuticals, wherein said at least two radiopharmaceuticals are:

Tc-99m-dihydrogen methylenediphosphate (medronate); and  
In-111-white blood cells.

421. The kit of claim 420, wherein a dose of said Tc-99m-dihydrogen methylenediphosphate (medronate) is up to about 15 mCi and a dose of said In-111-white blood cells is up to about 2 mCi.

422. A kit comprising at least two compositions for generating at least two radiopharmaceuticals, wherein said at least two radiopharmaceuticals are:

gallium-67; and  
In-111-white blood cells.

423. The kit of claim 422, wherein a dose of said gallium-67 is up to about 5 mCi and a dose of said In-111-white blood cells is up to about 2 mCi.

424. A kit comprising at least two compositions for generating at least two radiopharmaceuticals, wherein said at least two radiopharmaceuticals are:

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Tc-99m-teboroxime Tl-201-thallous chloride; and  
In-111-annexin.

425. The kit of claim 424, wherein a dose of said Tc-99m-teboroxime is up to about 15 mCi, a dose of said Tl-201-thallous chloride is up to about 2 mCi, and a dose of said In-111-annexin is up to about 2 mCi.

426. A kit comprising at least two compositions for generating at least two radiopharmaceuticals, wherein said at least two radiopharmaceuticals are:  
Tl-201-thallous chloride; and  
Tc-99m-pyrophosphate.

427. The kit of claim 426, wherein a dose of said Tl-201-thallous chloride is up to about 2 mCi and a dose of said Tc-99m-pyrophosphate is up to about 15 mCi.

428. Use of F-18-Fluorodeoxyglucose (FDG), as a substrate for hexokinase in glucose metabolism, for the study of glucose metabolism of cells including tumor, heart and brain cells.

429. Use of F-18-Fluoromisonidazole for imaging of hypoxia and oxidative metabolism, with the clinical application of radiotherapy treatment planning.

430. Use of F-18-3'-Fluoro-3'-deoxythymidine (FLT) for the study of DNA synthesis.

431. Use of F-18-Fluoromethyl choline (FCH) as a choline precursor for cell membrane synthesis, for the study of choline metabolism of tumors.

432. Use of F-18-4-Fluoro-m-tyrosine (FMT) as a precursor for dopamine synthesis and as a substrate for aromatic amino acid decarboxylase (AAAD), with the clinical application of imaging brain tumors.

433. Use of F-18-6-Fluoro-L-DOPA as a precursor for dopamine synthesis and as a precursor for AAAD, with the clinical applications of imaging and grading Parkinson's disease and imaging neuroendocrine tumors.

434. Use of F-18-FP- $\beta$ -CIT for binding to the dopamine transporter in dopaminergic axons, with the clinical application of imaging and grading Parkinson's disease and imaging neuroendocrine tumors.

435. Use of F-18-Pencyclovir (FHBG) to target thymidine kinase, with the clinical application of imaging reporter gene expression.

436. Use of F-18-Fuoroestradiol (FES) to target estrogen receptors, with the clinical application of breast tumor imaging.

437. Use of C-11-Methionine to target amino acid synthesis, with the clinical application of imaging brain tumors.

438. Use of Tc-99m-P280, Acutect® to target GP IIb/IIIa receptors on platelets, with the clinical applications of detection of thrombosis, such as deep vein thrombosis (DVT) and intrarterial thrombosis in coronary and carotid arteries.

439. Use of C-11-Raclopride to target dopamine D2 receptors, for brain imaging of dopamine D2 receptors in schizophrenia, and assessment of dose for neuroleptics.

440. Use of I-123-iodobenzamide (IBZM) to target dopamine D2 receptors, for brain imaging of dopamine D2 receptors in schizophrenia, and assessment of dose for neuroleptics.

441. C-11-carfentanil to target Mu opioid receptors in brain, with the clinical application of imaging drug addiction.

442. Use of C-11- $\alpha$ -methyl-L-tryptophan as a precursor for  $\alpha$ -methyl serotonin synthesis and as a substrate for AAAD enzyme, with the clinical application of imaging depression.

443. Use of C-11-5-Hydroxytryptophan as a precursor for serotonin synthesis with the clinical application of imaging neuroendocrine tumors.

444. Use of F-18-MPPF to bind to 5-HT<sub>1A</sub> (5-hydroxytryptamine-1A) serotonin receptors, with the clinical application of imaging depression and epilepsy.

445. Use of F-18-Altanserin to bind to 5-HT<sub>2A</sub> serotonin receptors with the clinical application of imaging depression and epilepsy.

446. Use of C-11-Acetate for the study of tricarboxylic acid cycle activity and oxidative metabolism with the clinical application of studying myocardial oxygen metabolism.

447. Use of C-11-Palmitate as a precursor for fatty acid metabolism with the clinical application of imaging myocardial metabolism.

448. Use of F-18-Fluorodopamine to target presynaptic adrenergic receptors.

449. A method for treating a patient, comprising:  
(a) applying a therapy to the patient;  
(b) performing on the patient a functional imaging procedure according to a method, kit or composition of any of claims 1-427 to measure a property indicative of biochemical activity of at least one tissue of the patient; and  
modifying at least one parameter of the therapy responsively to the measured biochemical activity.

450. The method according to claim 449, wherein performing the imaging procedure comprises performing a SPECT imaging procedure on the patient.

451. The method according to claim 450, wherein performing the SPECT imaging procedure comprises performing the SPECT imaging procedure using a high-definition SPECT camera.

452. The method according to claim 449, wherein said therapy comprises a therapeutic radiopharmaceutical.

453. Apparatus for use with any of a method, kit or composition of any of claims 1-427, the apparatus comprising:

a container containing at least one radiopharmaceutical of a method, kit or composition of any of claims 1-427; and

a portable computer-communicatable data carrier associated with the container, the data carrier containing imaging protocol information of a method, kit or composition of any of claims 1-427 for use with the at least one radiopharmaceutical.

454. The apparatus according to claim 453, wherein the apparatus comprises a device configured to write the imaging protocol information to the data carrier.

455. The apparatus according to claim 453, wherein the data carrier additionally contains administration protocol information useful for administering the at least one radiopharmaceutical.

456. The apparatus according to claim 453, wherein the imaging protocol information comprises instructions for performing an imaging procedure using the at least one radiopharmaceutical.

457. The apparatus according to claim 453, wherein the imaging protocol information comprises an identifier of an imaging protocol.

458. The apparatus according to claim 453, wherein the imaging protocol information comprises a parameter of the at least one radiopharmaceutical.

459. The apparatus according to claim 453, wherein the imaging protocol information comprises a parameter useful for configuring at least one aspect of an imaging procedure performed using the at least one radiopharmaceutical.

460. The apparatus according to claim 453, wherein the container contains a single dose of the radiopharmaceutical agent, which dose is appropriate for use with the imaging protocol information.

461. The apparatus according to claim 453, wherein the container contains a plurality of radiopharmaceuticals mixed together.

462. The apparatus according to claim 453, wherein the container is shaped so as to define a plurality of chambers, each of which contains a respective one of a plurality of radiopharmaceuticals.

463. The apparatus according to any one of claims 453-462, wherein the data carrier comprises a first data carrier, which contains a first identifier value,

wherein the apparatus further comprises a second computer-communicatable data carrier, which contains a second identifier value, and

wherein the apparatus is configured to operate responsively to a detection of a correspondence between the first and second identifier values.

464. The apparatus according to claim 463, wherein at least one of the first and second data carriers is configured to perform the detection of the correspondence.

465. The apparatus according to claim 463, wherein the apparatus comprises a correspondence-detection element configured to perform the detection of the correspondence.

466. The apparatus according to claim 463, wherein at least one of the first and second data carriers contains an identifier of a patient to whom the radiopharmaceutical is to be administered.

467. The apparatus according to claim 463, wherein at least one of the first and second identifier values comprises an identifier of a patient to whom the radiopharmaceutical is to be administered.

468. The apparatus according to claim 463, wherein exactly one of the first and second data carriers comprises a coupling mechanism configured to be coupled to a patient to whom the radiopharmaceutical is to be administered.

469. The apparatus according to claim 463, wherein the apparatus comprises an imaging system comprising imaging functionality, the imaging system configured, responsively to the detection of the correspondence, to drive the imaging functionality to perform an imaging procedure using the at least one radiopharmaceutical.

470. The apparatus according to any one of claims 453-462, wherein the data carrier is physically coupled to the container.

471. The apparatus according to claim 470, wherein the data carrier contains an identifier of a patient to whom the radiopharmaceutical is to be administered, and wherein the imaging protocol information comprises imaging protocol information selected for the patient.

472. The apparatus according to claim 471, wherein the imaging protocol information comprises an identifier of an imaging protocol.

473. The apparatus according to claim 471, wherein the imaging protocol information comprises imaging protocol information customized for the patient.



474. The apparatus according to any one of claims 453-63, wherein the imaging protocol information comprises SPECT imaging protocol information.

475. The apparatus according to claim 474, wherein the SPECT imaging protocol information comprises dynamic SPECT imaging protocol information.

476. The apparatus according to claim 475, wherein the SPECT imaging protocol information comprises at least one kinetic parameter of the at least one radiopharmaceutical, the at least one kinetic parameter useful for performing a dynamic SPECT imaging procedure using the at least one radiopharmaceutical.

477. The apparatus according to any one of claims 453-462, comprising an imaging system, which comprises:  
a communication element, configured to read the imaging protocol information from the data carrier; and  
a control unit, comprising imaging functionality, which is configured to perform an imaging procedure, and to configure the procedure at least in part responsively to the imaging protocol information read from the data carrier by the communication element.

478. The apparatus according to claim 477, wherein the imaging system comprises a camera, wherein the imaging functionality comprises image acquisition functionality, and wherein the image acquisition functionality is configured to perform an image acquisition procedure using the camera, and to configure the procedure at least in part responsively to the imaging protocol information read from the data carrier by the communication element.

479. The apparatus according to claim 478, wherein the image acquisition functionality configures a total acquisition time of the image acquisition procedure at least in part responsively to the imaging protocol information.

480. The apparatus according to claim 478, wherein the camera comprises a plurality of detectors, and wherein the image acquisition functionality is configured to

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configure, at least in part responsively to the imaging protocol information, at least one motion of at least one of the detectors during the image acquisition procedure.

481. The apparatus according to claim 478, wherein the control unit is configured to configure, at least in part responsively to the imaging protocol information, a waiting time between administration of the radiopharmaceutical and commencement of the image acquisition procedure.

482. The apparatus according to claim 478, wherein the image acquisition functionality is configured to perform a gated image acquisition procedure at least in part responsively to the imaging protocol information.

483. The apparatus according to claim 477, wherein the imaging functionality comprises image reconstruction functionality, and wherein the image reconstruction functionality is configured to perform an image reconstruction procedure, and to configure the procedure at least in part responsively to the imaging protocol information read from the data carrier by the communication element.

484. The apparatus according to claim 477, wherein the imaging functionality comprises image analysis functionality, and wherein the image analysis functionality is configured to perform an image analysis procedure, and to configure the procedure at least in part responsively to the imaging protocol information read from the data carrier by the communication element.

485. The apparatus according to claim 477, wherein the imaging functionality comprises diagnosis functionality, and wherein the diagnosis functionality is configured to perform a diagnostic procedure, and to configure the procedure at least in part responsively to the imaging protocol information read from the data carrier by the communication element.

486. The apparatus according to claim 477, wherein the imaging procedure includes a three-dimensional dynamic imaging study, and wherein the imaging functionality is configured to perform the three-dimensional dynamic imaging study,

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and to configure the study at least in part responsively to the imaging protocol information read from the data carrier by the communication element.

487. The apparatus according to any one of claims 453-462, wherein the data carrier is not physically coupled to the container, and wherein the data carrier contains an identifier of a patient to whom the radiopharmaceutical is to be administered.

488. The apparatus according to claim 487, wherein the data carrier comprises a coupling mechanism configured to be coupled to the patient.

489. The apparatus according to claim 487, wherein the data carrier comprises a first data carrier, and wherein the apparatus further comprises a second computer-communicatable data carrier physically coupled to the container, the second data carrier containing radiopharmaceutical information regarding the at least one radiopharmaceutical.

490. Apparatus for use with at least one radiopharmaceutical of a method, kit or composition of any of claims 1-427, the apparatus comprising:

- a container containing the at least one radiopharmaceutical; and

- a computer-communicatable data carrier associated with the container, the data carrier containing authenticatable information regarding a commercial license for use of the imaging protocol information of any of the methods of claims 1-384 with the at least one radiopharmaceutical.

491. The apparatus according to claim 490, comprising an imaging system, which comprises:

- a communication element, configured to read the authenticatable license information from the data carrier;

- a control unit, comprising imaging functionality, the control unit configured to:

- authenticate the authenticatable license information, and

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only upon authentication, drive the imaging functionality to perform an imaging procedure using the SPECT imaging protocol information.

492. The apparatus according to claim 490, wherein the apparatus comprises a device configured to write the authenticatable license information to the data carrier.

493. The apparatus according to any one of claims 490-492, wherein the data carrier is physically coupled to the container.

494. Apparatus comprising a portable computer-communicatable data carrier containing authenticatable information regarding a commercial license for use of any of the imaging methods, kits or compositions of any of claims 1-427.

495. The apparatus according to claim 494, wherein the data carrier additionally contains patient information regarding a patient upon whom an imaging procedure using the SPECT imaging protocol information is to be performed.

496. The apparatus according to claim 494, wherein the authenticatable license information is encrypted.

497. The apparatus according to claim 494, wherein the apparatus comprises a device configured to write the authenticatable license information to the data carrier.

498. The apparatus according to claim 494, wherein the data carrier comprises a coupling mechanism configured to be coupled to a patient upon whom an imaging procedure using the SPECT imaging protocol information is to be performed.

499. The apparatus according to any one of claims 494-498, comprising an imaging system, which comprises:

a communication element, configured to read the authenticatable license information from the data carrier;

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a control unit, comprising imaging functionality, the control unit configured to:

authenticate the authenticatable license information, and  
only upon authentication, drive the imaging functionality to perform an imaging procedure using the SPECT imaging protocol information.

500. Apparatus for use with at least one radiopharmaceutical of a method, kit or composition of any of claims 1-427 for administration to a patient, the apparatus comprising:

a container containing the at least one radiopharmaceutical;  
a first computer-communicatable data carrier physically coupled to the container, the first data carrier containing radiopharmaceutical information regarding the at least one radiopharmaceutical; and  
a second portable computer-communicatable data carrier containing patient information regarding the patient, and imaging protocol information for use with the at least one radiopharmaceutical.

501. The apparatus according to claim 500, wherein the imaging protocol information comprises SPECT imaging protocol information.

502. The apparatus according to claim 500, wherein the patient information comprises an identifier of the patient.

503. The apparatus according to claim 500, wherein the second data carrier comprises a coupling mechanism configured to be coupled to the patient.

504. The apparatus according to claim 500, wherein the first data carrier contains a first patient identifier, wherein the patient information contained in the second data carrier comprises a second patient identifier, and comprising an administration system, which comprises:

a first communication element, configured to read the first patient identifier from the first data carrier;

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a second communication element, configured to read the second patient identifier from the second data carrier; and

a control unit, configured to compare the first patient identifier to the second patient identifier, and, upon detecting a match, generate an administration signal that triggers administration to the patient of the at least one radiopharmaceutical contained in the container.

505. The apparatus according to claim 500, wherein the first data carrier contains a first protocol identifier, wherein the imaging protocol information contained in the second data carrier comprises a second protocol identifier, and comprising an administration system, which comprises:

a communication element, configured to read the first and second protocol identifiers from the first and second data carriers, respectively; and

a control unit, configured to compare the first protocol identifier to the second protocol identifier, and, upon detecting a match, generate an administration signal that triggers administration to the patient of the at least one radiopharmaceutical contained in the container.

506. The apparatus according to claim 500, wherein the first data carrier contains a first protocol identifier, wherein the imaging protocol information contained in the second data carrier comprises a second protocol identifier, and comprising an administration system, which comprises:

a first communication element, configured to read the first protocol identifier from the first data carrier;

a second communication element, configured to read the second protocol identifier from the second data carrier; and

a control unit, configured to compare the first protocol identifier to the second protocol identifier, and, upon detecting a match, generate an administration signal that triggers administration to the patient of the at least one radiopharmaceutical contained in the container.

507. The apparatus according to claim 500, comprising an administration system, which comprises:

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a communication element; and  
a control unit, configured to:  
generate an administration signal that triggers administration to the patient of  
the at least one radiopharmaceutical contained in the container, and  
drive the communication element to transmit information regarding the  
administration to the second data carrier.

508. The apparatus according to claim 500, wherein the apparatus comprises a device configured to write the imaging protocol information to the first data carrier.

509. The apparatus according to claim 500, wherein the apparatus comprises a device configured to write the patient information to the second data carrier.

510. The apparatus according to any one of claims 500-509, wherein the imaging protocol information comprises imaging protocol information selected for the patient.

511. The apparatus according to claim 510, wherein the imaging protocol information comprises an identifier of an imaging protocol.

512. The apparatus according to claim 511, wherein the imaging protocol information comprises imaging protocol information customized for the patient.

513. The apparatus according to any one of claims 500-509, wherein the first data carrier contains a first patient identifier, wherein the patient information contained in the second data carrier includes a second patient identifier, and comprising an administration system, which comprises:

a communication element, configured to read the first and second patient identifiers from the first and second data carriers, respectively; and

a control unit, configured to compare the first patient identifier to the second patient identifier, and, upon detecting a match, generate an administration signal that



triggers administration to the patient of the at least one radiopharmaceutical contained in the container.

514. The apparatus according to claim 513, wherein the administration system comprises an automated administration device, configured to administer the at least one radiopharmaceutical to the patient upon being triggered by the administration signal.

515. The apparatus according to claim 513, wherein the control unit is configured to generate the administration signal to trigger the administration of the at least one radiopharmaceutical by instructing a healthcare worker to administer the at least one radiopharmaceutical to the patient.

516. Apparatus for use with any of the imaging methods, kits and compositions of claims 1-427, the apparatus comprising:

- a container containing the at least one radiopharmaceutical;

- a computer-communicatable data carrier associated with the container, the data carrier containing data regarding at least one of: the radiopharmaceutical and the patient; and

- a SPECT imaging system comprising:

- a communication element, configured to read the data; and

- a control unit, configured to utilize the read data to customize at least one function of the system selected from the group consisting of: administration of the radiopharmaceutical, acquisition of a SPECT image of the patient to whom the radiopharmaceutical is administered, reconstruction of the SPECT image, analysis of the SPECT image, and diagnosis of a condition of the patient based at least in part on the analysis.

517. The apparatus according to claim 516, wherein the data carrier contains the data regarding the radiopharmaceutical.

518. The apparatus according to claim 516, wherein the data carrier contains the data regarding the patient.

519. The apparatus according to claim 516, wherein the control unit is configured to utilize the read data to customize the administration of the radiopharmaceutical.

520. The apparatus according to claim 516, wherein the control unit is configured to utilize the read data to customize the acquisition of a SPECT image of the patient to whom the radiopharmaceutical is administered.

521. The apparatus according to claim 516, wherein the control unit is configured to utilize the read data to customize the reconstruction of the SPECT image.

522. The apparatus according to claim 516, wherein the control unit is configured to utilize the read data to customize the analysis of the SPECT image.

523. The apparatus according to claim 516, wherein the control unit is configured to utilize the read data to customize the diagnosis of a condition of the patient based at least in part on the analysis.

524. The apparatus according to any one of claims 516-24, wherein the apparatus comprises a device configured to write the data to the data carrier.

525. A SPECT imaging system for use with a container containing at least one radiopharmaceutical for administration to a patient according to the method of any of claims 1-384, and data regarding at least one of: the radiopharmaceutical and the patient, the system comprising:

a communication element, configured to read the data; and

a control unit, configured to utilize the read data to customize at least one function of the system selected from the group consisting of: administration of the radiopharmaceutical, acquisition of a SPECT image of the patient to whom the radiopharmaceutical is administered, reconstruction of the SPECT image, analysis of

the SPECT image, and diagnosis of a condition of the patient based at least in part on the analysis.

526. The system according to claim 525, wherein the system comprises a device configured to write the data to the container.

527. An automated radiopharmaceutical dispensing system for use with a container and a computer-communicatable container data carrier associated with the container and for using of any of the kits or compositions and/or executing any of the methods of any of the claims 1-427, the system comprising:

- a robot, configured to manipulate the container;

- a communication element; and

- a control unit, configured to:

- receive radiopharmaceutical information regarding at least one radiopharmaceutical, the radiopharmaceutical information selected from the group consisting of: imaging protocol information for use with the at least one radiopharmaceutical, and authenticatable information regarding a commercial license for use of an imaging protocol with the at least one radiopharmaceutical,

- receive patient information regarding a patient,

- drive the robot to automatically dispense a dose of the radiopharmaceutical to the container, and

- drive the communication element to transmit to the container data carrier at least a portion of the radiopharmaceutical information and at least a portion of the patient information.

528. The system according to claim 527, wherein the control unit is configured to receive the radiopharmaceutical information regarding a plurality of radiopharmaceuticals, and drive the robot to automatically dispense respective doses of the radiopharmaceuticals to the container.

529. The system according to claim 527, wherein the patient information includes an identifier of an imaging protocol assigned to the patient for performance

using the dose, and wherein the control unit is configured to drive the communication element to transmit the imaging protocol identifier to the container data carrier.

530. The system according to claim 527, wherein the control unit is configured to drive the communication element to transmit to the container data carrier at least one of: a time of dispensing of the radiopharmaceutical to the container, and information regarding a radioactivity of the dose at the time of dispensing.

531. The system according to claim 527, comprising:  
a mother vial that contains the radiopharmaceutical prior to dispensing thereof; and  
a computer-communicatable mother vial data carrier associated with the mother vial, which mother vial data carrier contains the radiopharmaceutical information, wherein the control unit is configured to receive the radiopharmaceutical information from the mother vial data carrier.

532. The system according to any one of claims 527-531, wherein the radiopharmaceutical information comprises the imaging protocol information.

533. The system according to claim 532, wherein the imaging protocol information comprises SPECT imaging protocol information.

534. The system according to claim 533, wherein the imaging protocol information comprises at least one kinetic parameter of the at least one radiopharmaceutical.

535. The system according to any one of claims 527-531, wherein the radiopharmaceutical information comprises the authenticatable information regarding the commercial license.

536. The system according to claim 535, wherein the information regarding the commercial license comprises information regarding the commercial license for use of a SPECT imaging protocol with the at least one radiopharmaceutical.

537. The system according to claim 535, wherein the control unit is configured to authenticate the authenticatable license information, and to drive the robot to automatically dispense the dose only upon authentication.

538. An imaging system for implementing any of the methods of claims 1-384 or using any of the kits of claims 388-427, the imaging system comprising a radioimaging camera, which comprises a plurality of solid state detectors, configured for independent movement during data acquisition.

539. An imaging system for implementing any of the methods or using any of the kits or composition of any of the claims 1-427 the system comprising a radioactive-emission-measuring-camera system which comprises:

a housing;

at least one detecting unit, located within the housing and adapted for at least one form of motion with respect to the housing;

at least one motion provider, in mechanical communication with the at least one detecting unit, for providing it with the at least one form of motion;

a controller, in signal communication with the at least one motion provider, for instructing it regarding said at least one form of motion of the at least one detecting unit, thus automatically providing said at least one detecting unit with said at least one form of motion.

540. The imaging system of claim 539, wherein the at least one detecting unit includes a plurality of detecting units, each detecting unit moving independently.

541. A diagnostic pharmaceutical kit comprising

- (i) a packaged dose unit of a first diagnostic radiopharmaceutical;
- (ii) a packaged dose unit of a second diagnostic radiopharmaceutical;
- (iii) a packaged dose unit of saline; and
- (iv) a packaged dose unit of a pharmacological stress agent.

542. The diagnostic pharmaceutical kit of claim 541, wherein said pharmacological stress agent is selected from the group consisting of adenosine, dipyridamole or dobutamine.

543. The diagnostic pharmaceutical kit of claim 541, wherein said packaged dose unit of said first diagnostic radiopharmaceutical is a low dose.

544. The diagnostic pharmaceutical kit of claim 543, wherein said low dose is about 2.5 mrem or less per kg body weight.

545. The diagnostic pharmaceutical kit of claim 543, wherein said first diagnostic radiopharmaceutical is Tc99.

546. The diagnostic pharmaceutical kit of claim 545, wherein said low dose is less than 6 mCi.

547. The diagnostic pharmaceutical kit of claim 541, wherein said packaged dose unit of said second diagnostic radiopharmaceutical is a high dose.

548. The diagnostic pharmaceutical kit of claim 547, wherein said second diagnostic radiopharmaceutical is Tc99.

549. The diagnostic pharmaceutical kit of claim 548, wherein said high dose is between 25-50 mCi.

550. The diagnostic pharmaceutical kit of claim 547, wherein said high dose is about 30 mrem or more per kg body weight.

551. The diagnostic pharmaceutical kit of claim 541, wherein each of said packaged dose units are associated with a portable computer-communicatable data carrier, the data carrier containing imaging protocol information for use with said packaged dose units.

552. A method of radioimaging a myocardial perfusion, the method comprising in sequence:

- (a) administering to a subject a low dose of a first radiopharmaceutical;
- (b) subjecting said subject to a physical stress;
- (c) administering to said subject at a peak of said physical stress a medium or high dose of a second radiopharmaceutical;
- (d) immediately radioimaging a heart of said subject, thereby radioimaging a myocardial perfusion.

553. The method of claim 552, wherein said first radiopharmaceutical and said second radiopharmaceutical are identical.

554. The method of claim 553, wherein said first radiopharmaceutical and said second radiopharmaceutical is Tc99.

555. The method of claim 552, wherein said first radiopharmaceutical and said second radiopharmaceutical are not identical.

556. The method of claim 552, wherein said first radiopharmaceutical is Tl201 and said second radiopharmaceutical is Tc99.

557. The method of claim 552, wherein said first radiopharmaceutical is Tl201 and said second radiopharmaceutical is Iodine 123.

558. The method of claim 552, wherein said first radiopharmaceutical is Tc99 and said second radiopharmaceutical is Iodine 123.

559. The method of claim 552, wherein a length of time of steps a-d is no more than 20 minutes.

560. The method of claim 552, wherein a length of time of steps a-d is no more than 30 minutes.



561. The method of claim 552, wherein the method comprises only one radioimaging step.

562. The method of claim 552, further comprising radiomaging a heart of said subject following step (a).

563. The method of claim 562, wherein the method takes less than 20 minutes.

564. The method of claim 552, wherein the method takes less than 30  
5 minutes.

565. The method of claim 552, wherein the method is effected as described in Tables 91 or 92.

566. A method of radioimaging a myocardial perfusion, the method comprising in sequence:

- (a) administering to a subject a radiopharmaceutical;
- (b) immediately radioimaging a heart of said subject, thereby radioimaging a myocardial perfusion.

567. The method of claim 566, wherein a length of time of steps a-b is no more than 10 minutes.

568. The method of claim 552 or 566, wherein said radioimaging takes less than 6 minutes.

569. The method of claim 562, wherein said further radioimaging takes less than 6 minutes.

570. The method of claim 568, wherein said radioimaging takes less than 3 minutes.

571. The method of claim 569, wherein said radioimaging takes less than 3 minutes.
572. The method of claim 552 or 566, wherein said radioimaging generates a 3D spectrum image and takes less than 6 minutes.
573. The method of claim 552 or 566, wherein said radioimaging comprises generation of multiple images at multiple time points post injection.
574. The method of claim 552 or 566, being effected under the camera.
575. The method of claim 573, wherein said multiple images generate information on turn-over kinetics.
576. The method of claim 552 or 566, being controlled in accordance with an information carrier attached to a container of said first and said second radiopharmaceutical.
577. The method of claim 576, wherein said administering is provided by an automatic injector which responds to a protocol information encrypted in said information carrier.
578. The method of any of claims 1-385 and 548-577, further comprising administering to the subject a trace amount of radiopharmaceutical prior to step (a).
579. The method of claim 578, wherein said trace amount is less than 2 mCi.
580. The method of claim 578, wherein said trace amount is less than 1 mCi.
581. The method of claim 576, further comprising radioimaging an organ of interest following said administering said trace amount of radiopharmaceutical.
582. The method of claim 581, wherein said further radioimaging generates a baseline intensity image of said radiopharmaceutical existing in the body.

583. A diagnostic pharmaceutical kit comprising
- (i) a packaged dose unit of a first diagnostic radiopharmaceutical; and
  - (ii) a packaged dose unit of saline.

584. A diagnostic pharmaceutical kit comprising
- (i) a packaged dose unit of a first diagnostic radiopharmaceutical; and
  - (ii) a packaged dose unit of a pharmacological stress agent.

585. The diagnostic pharmaceutical kit of claims 583 or 584, further comprising a second radiopharmaceutical.

586. The diagnostic pharmaceutical kit of claim 583, further comprising a pharmacological stress agent.

587. The diagnostic pharmaceutical kit of claim 584, further comprising a packaged dose unit of saline.

588. The diagnostic pharmaceutical kit of claims 583 or 584, wherein each of said packaged dose units are associated with a portable computer-communicatable data carrier, the data carrier containing imaging protocol information for use with said packaged dose units.

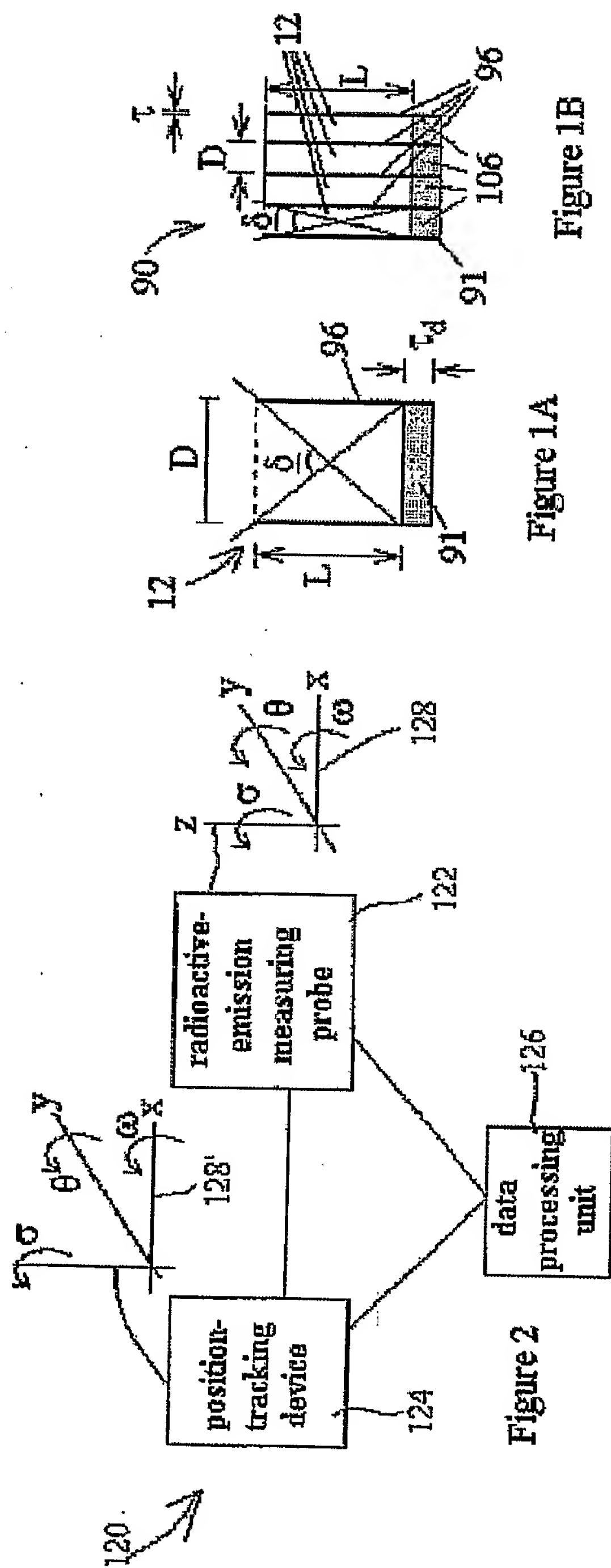


Figure 1B

Figure 1A

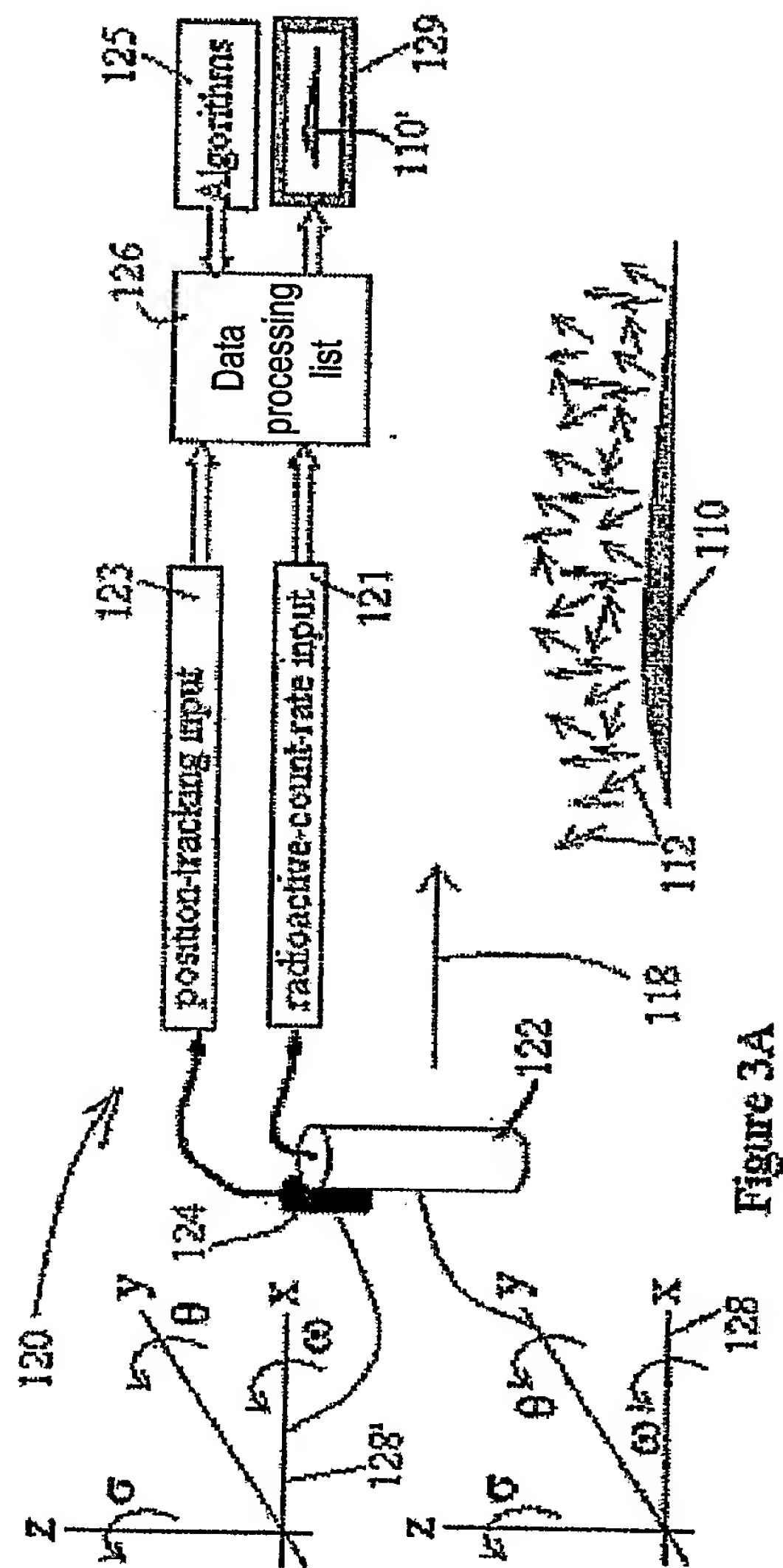


Figure 3A

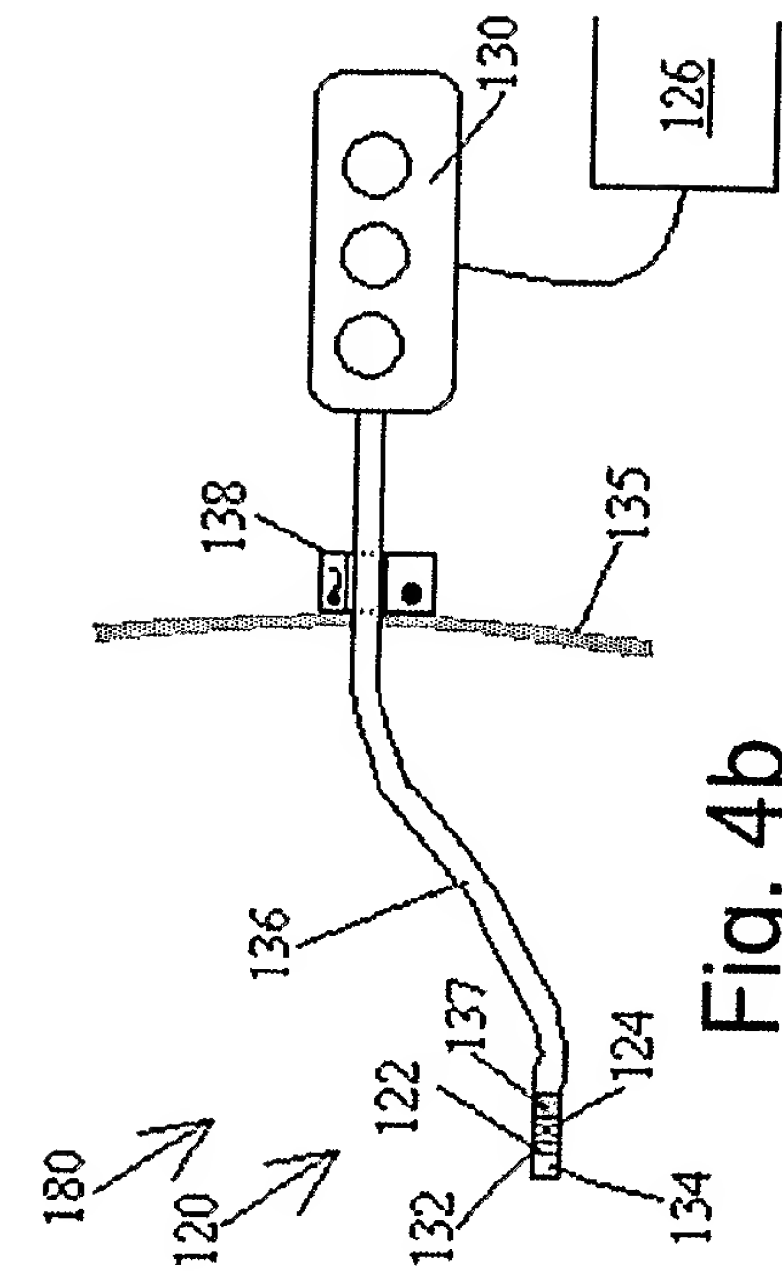
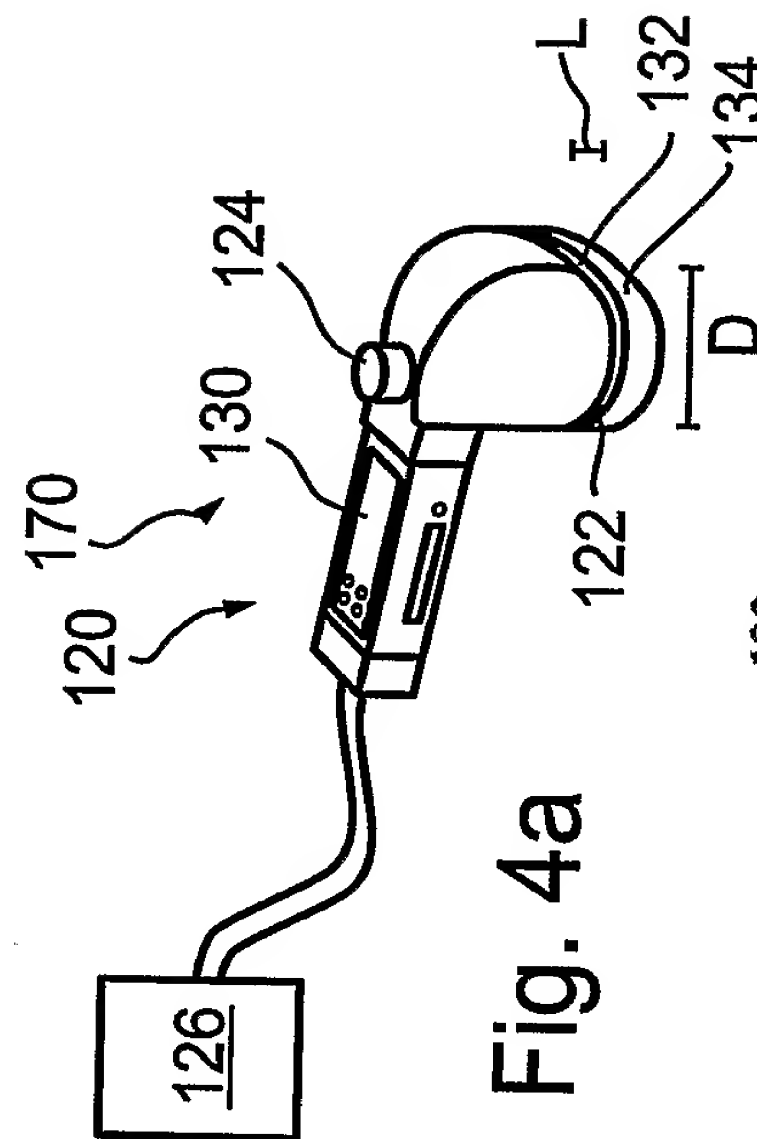


Fig. 4b



**Fig. 4a**

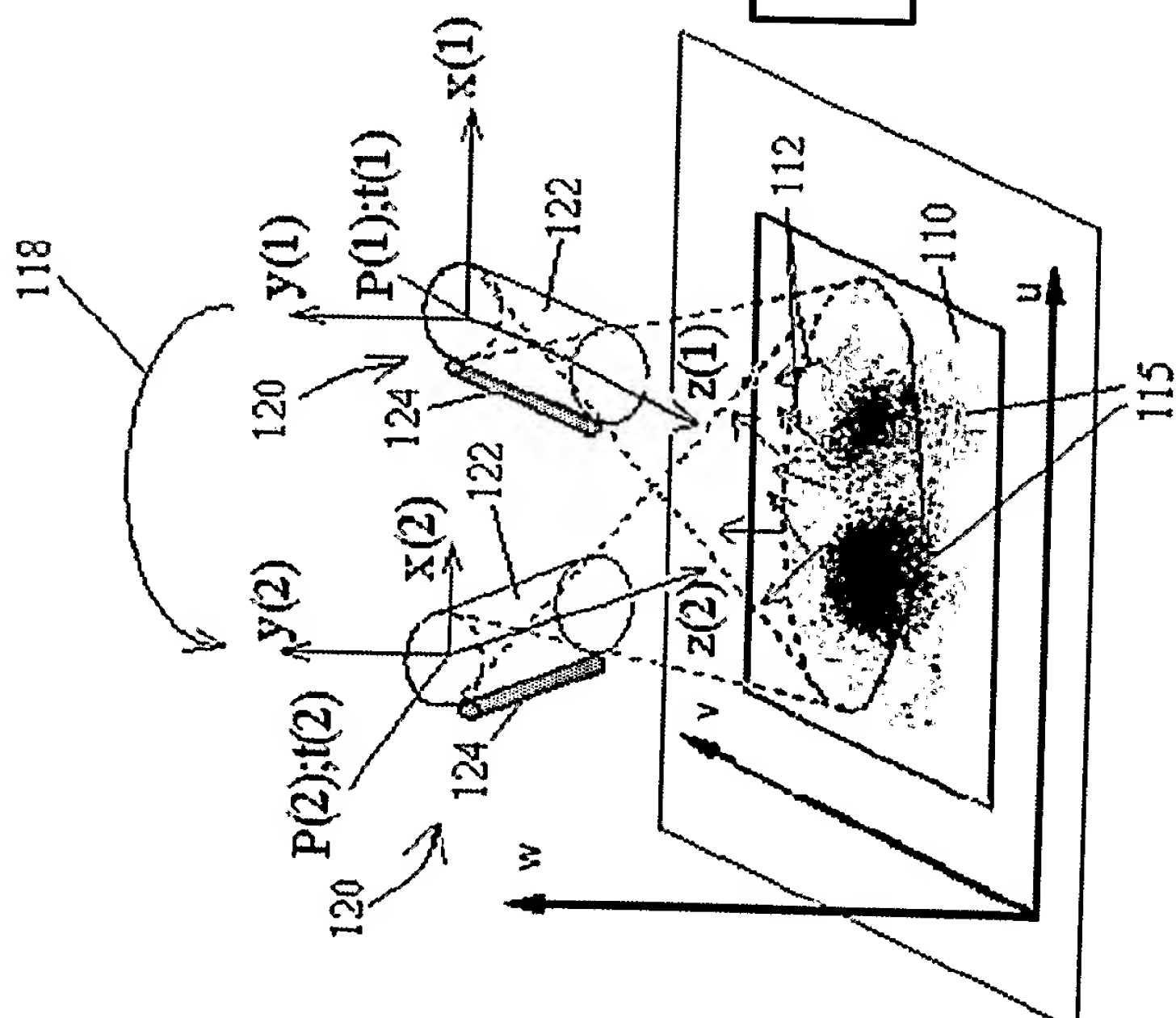


Fig. 3b

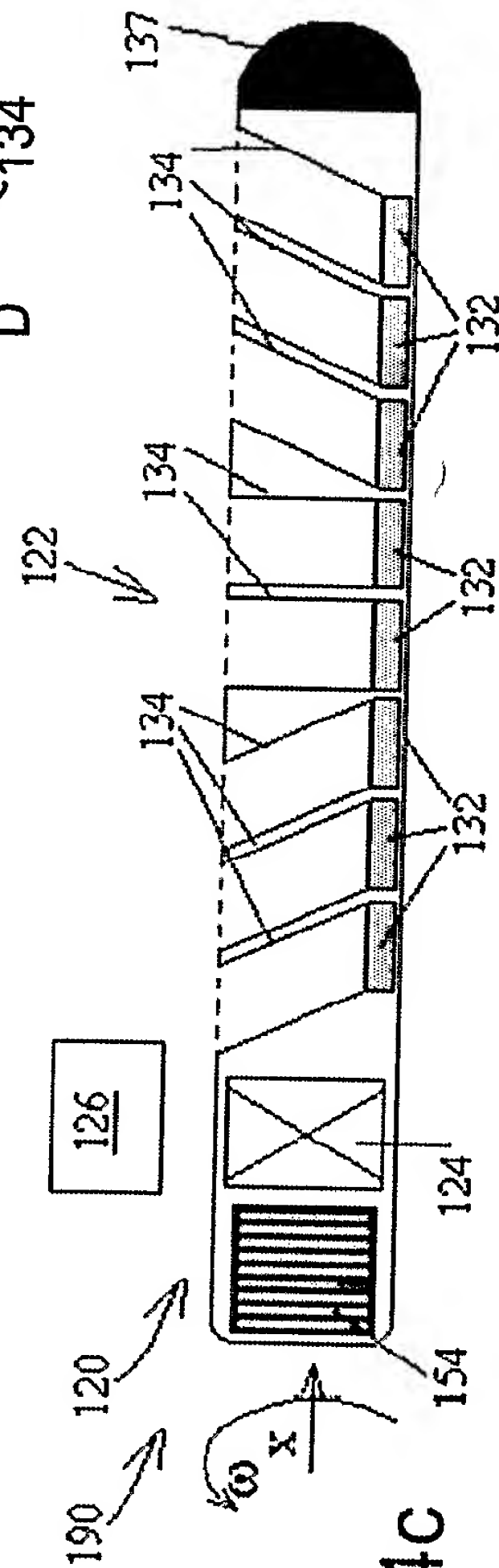
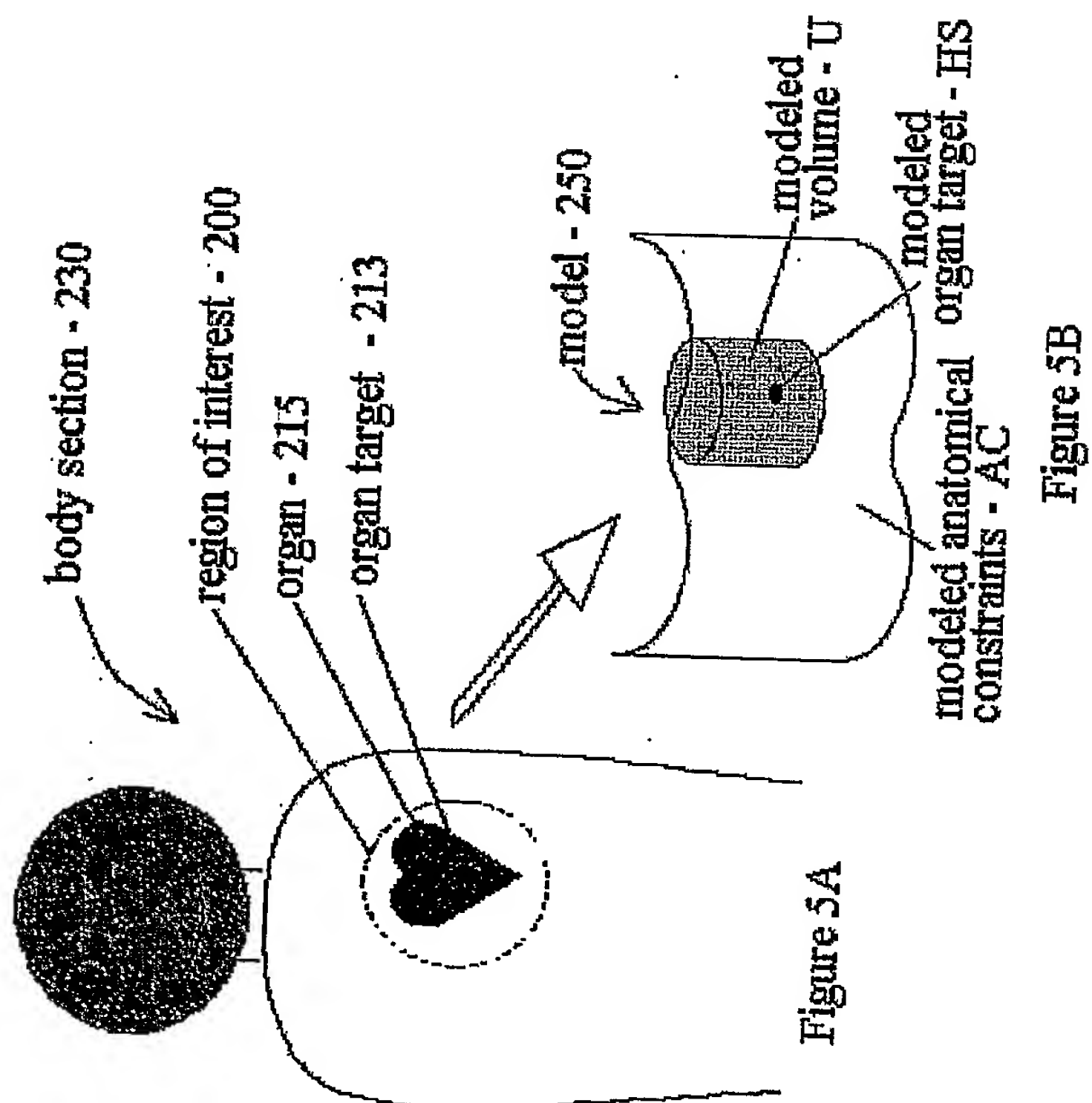
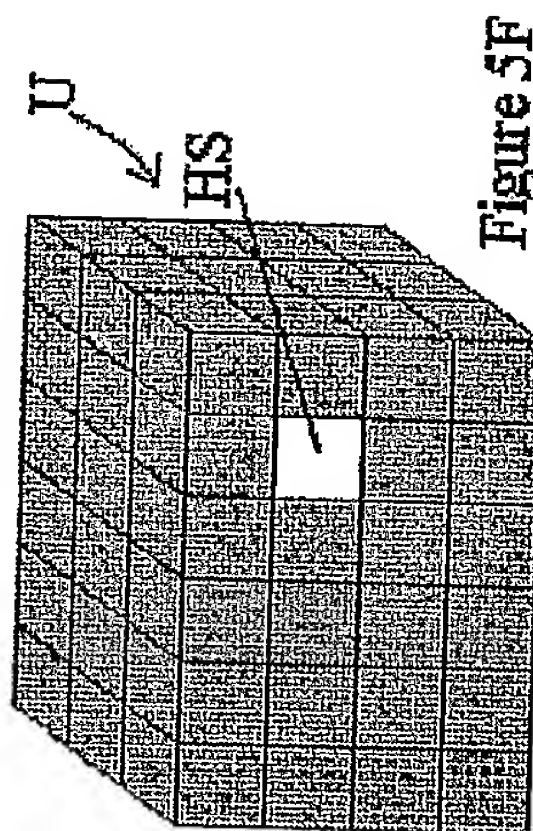
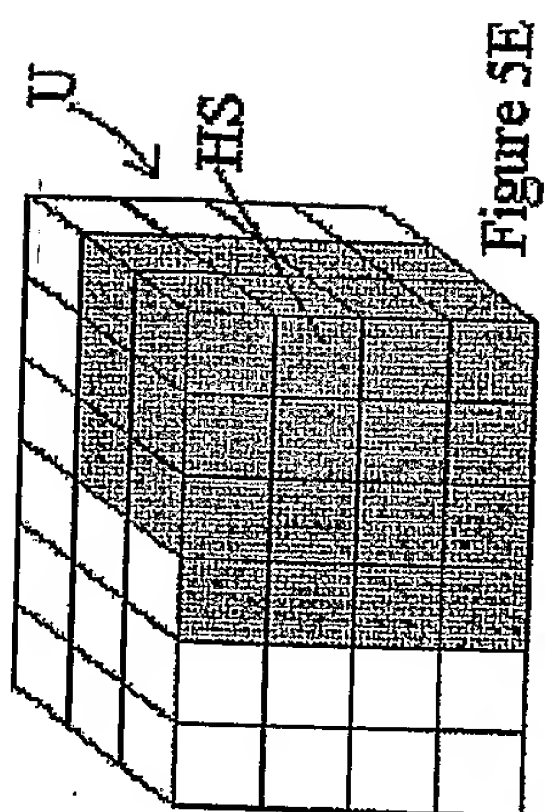
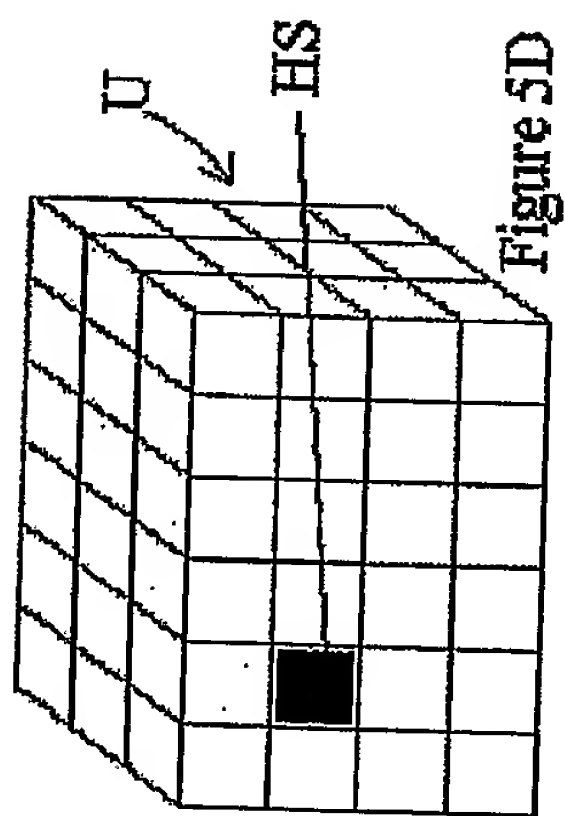
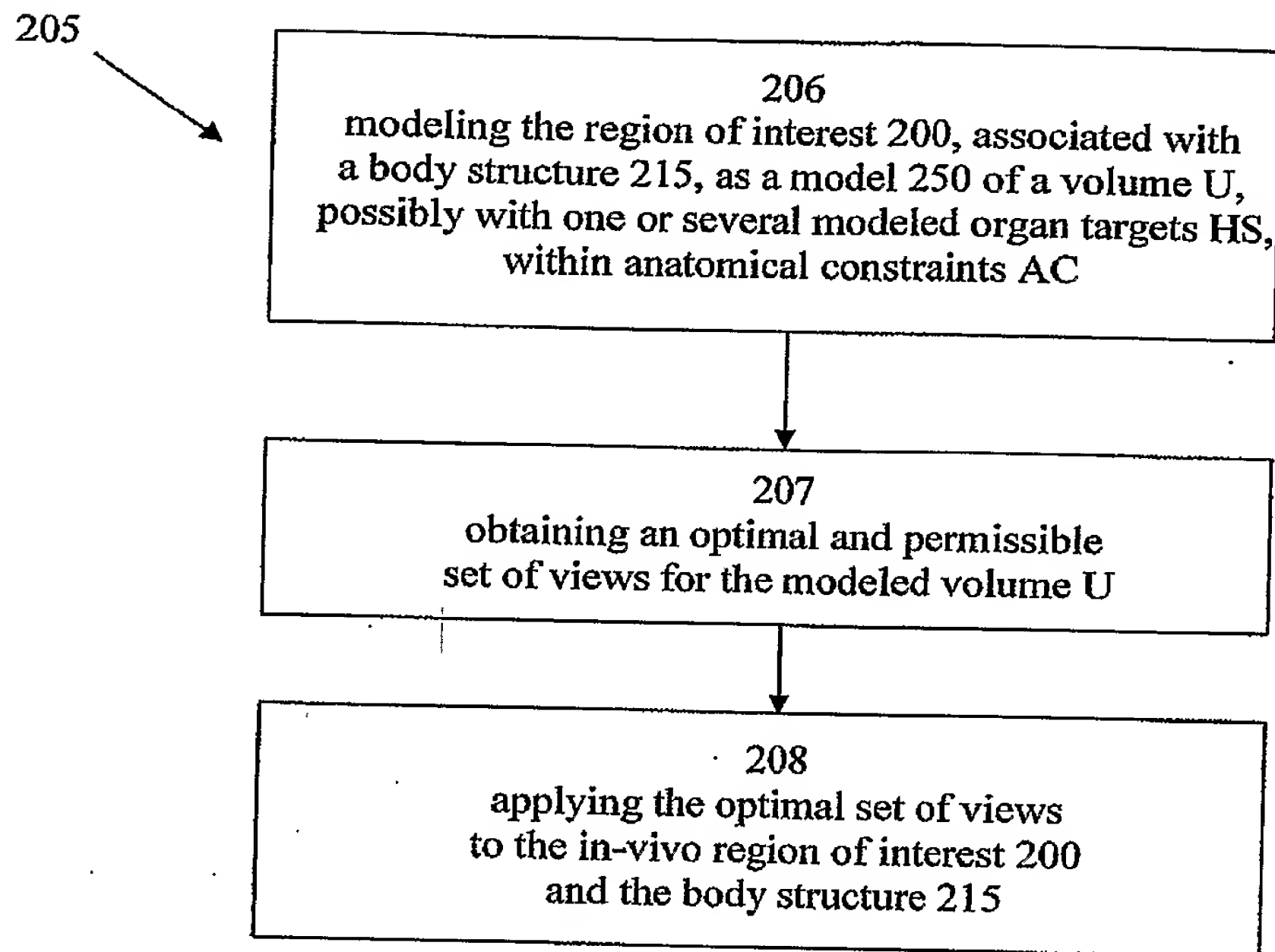


Fig. 4c



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Figure 5C





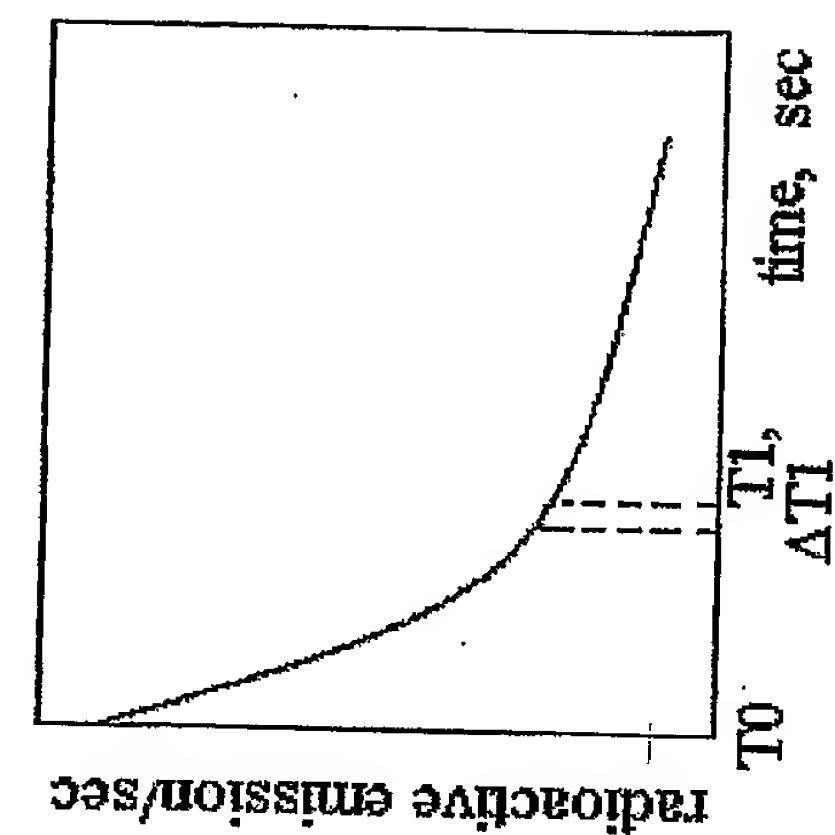
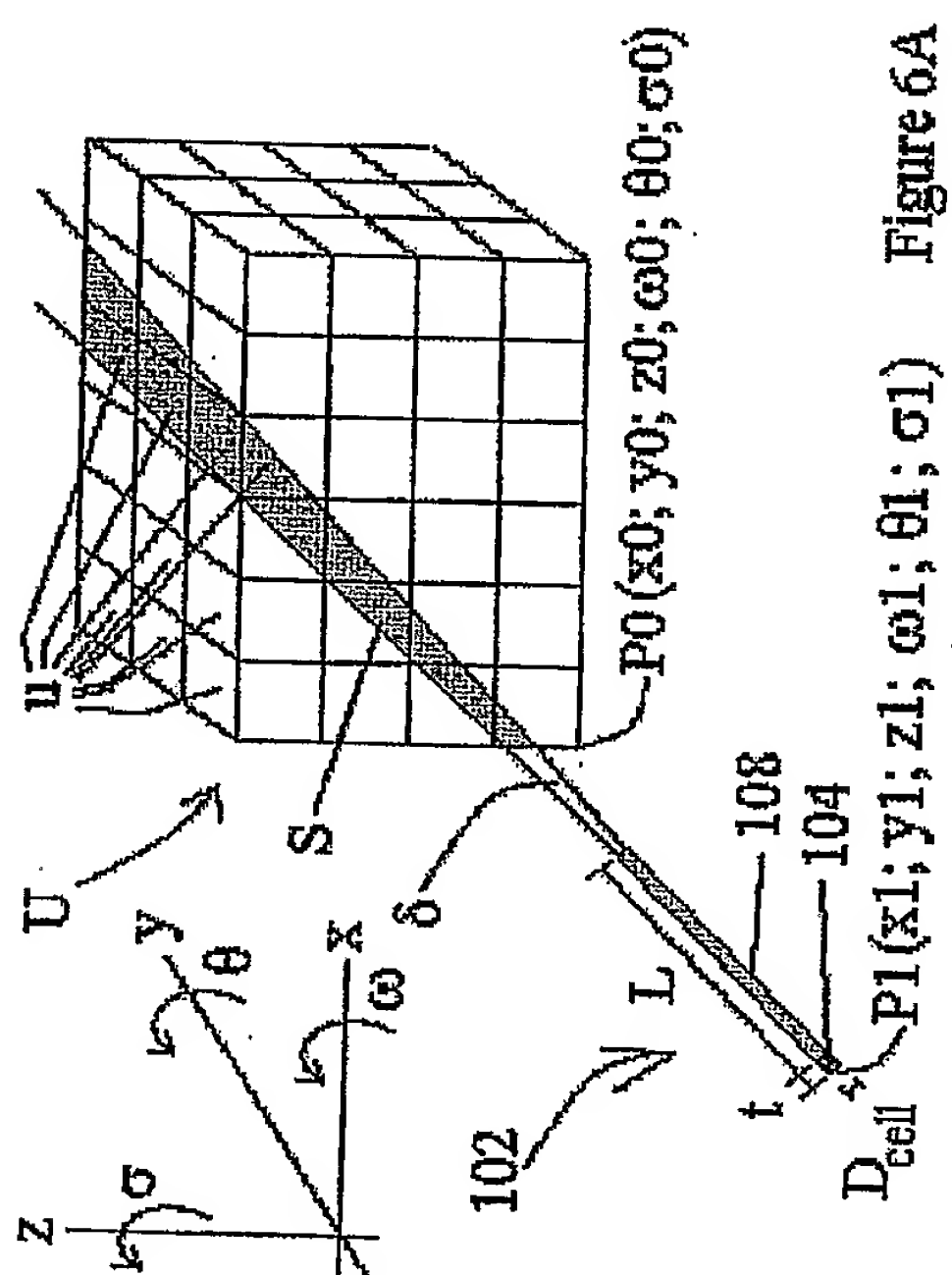
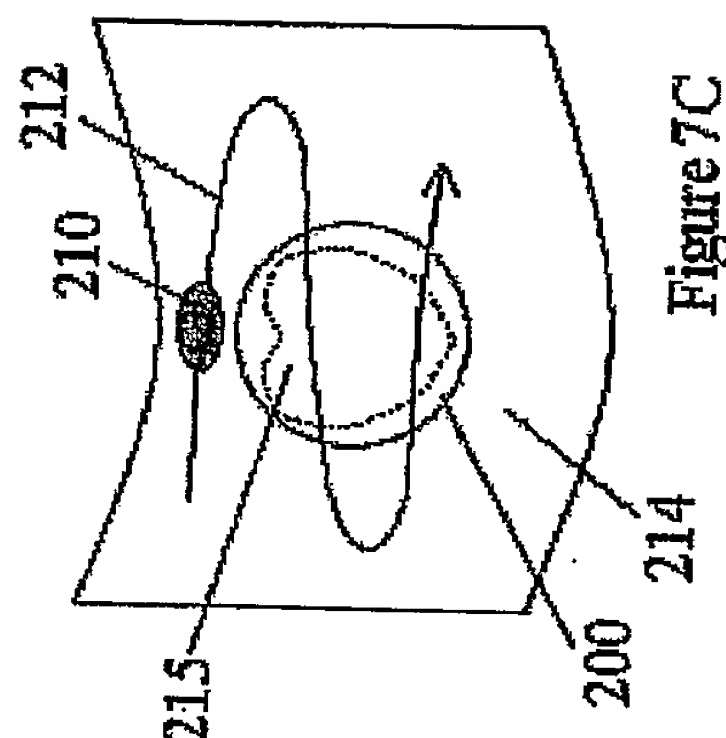


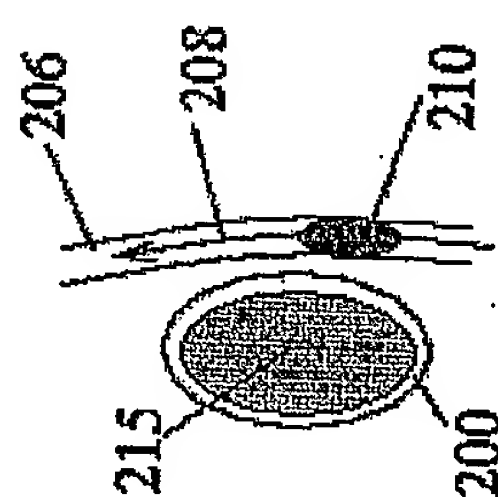
Figure 6B



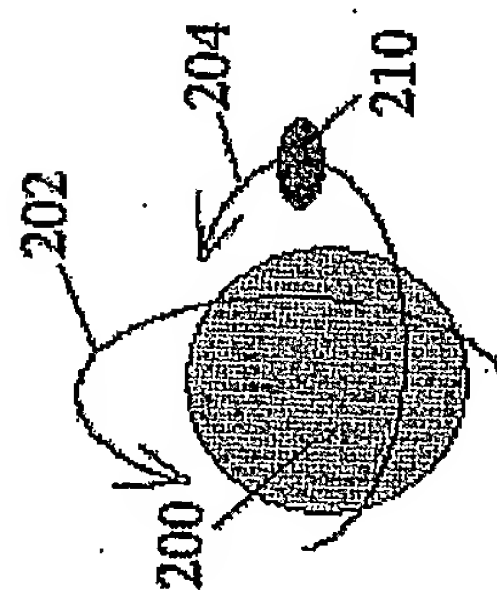
**Figure 6A**



**Figure 7C**



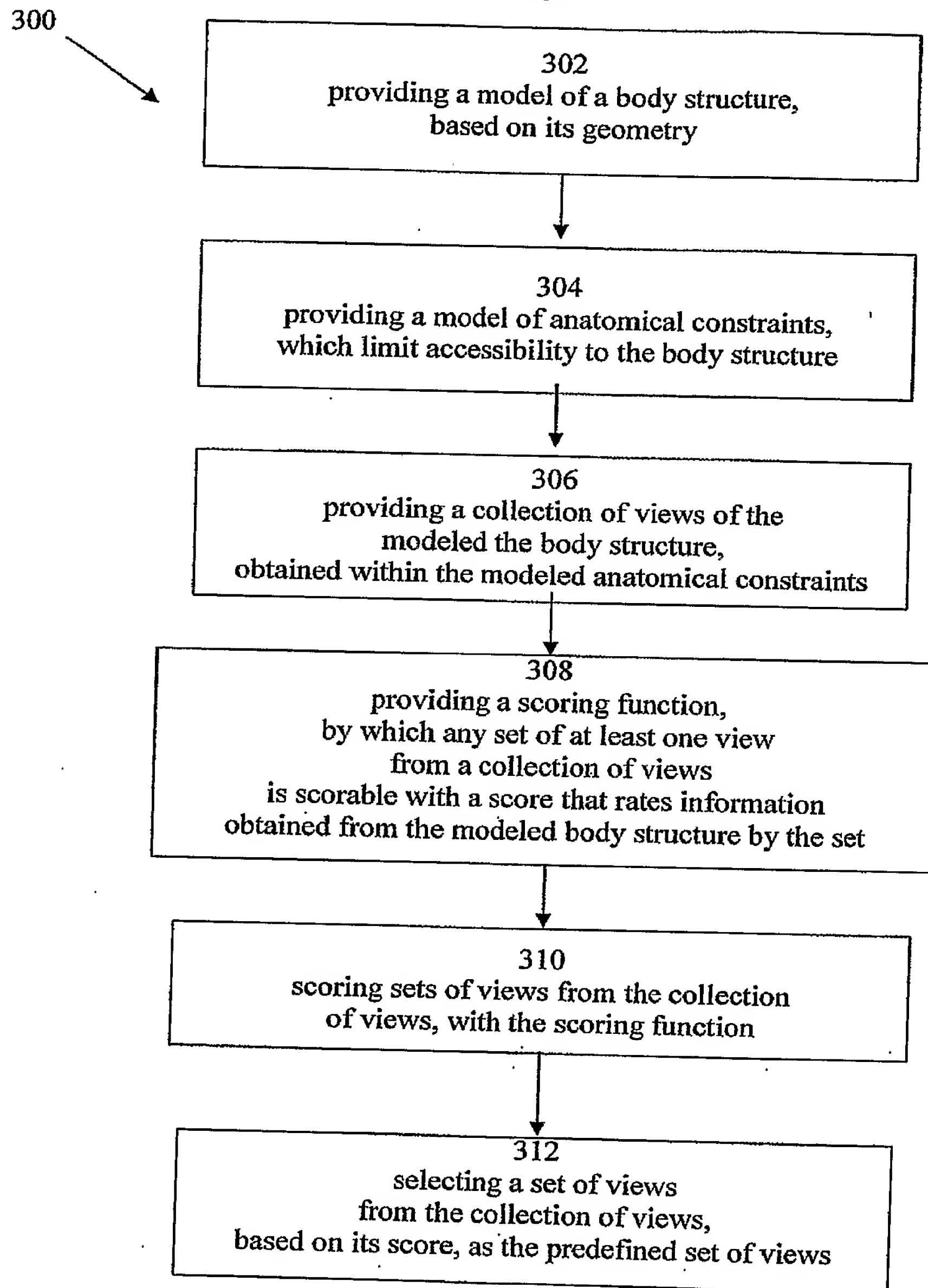
**Figure 7B**



**Figure 7A**

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Figure 8



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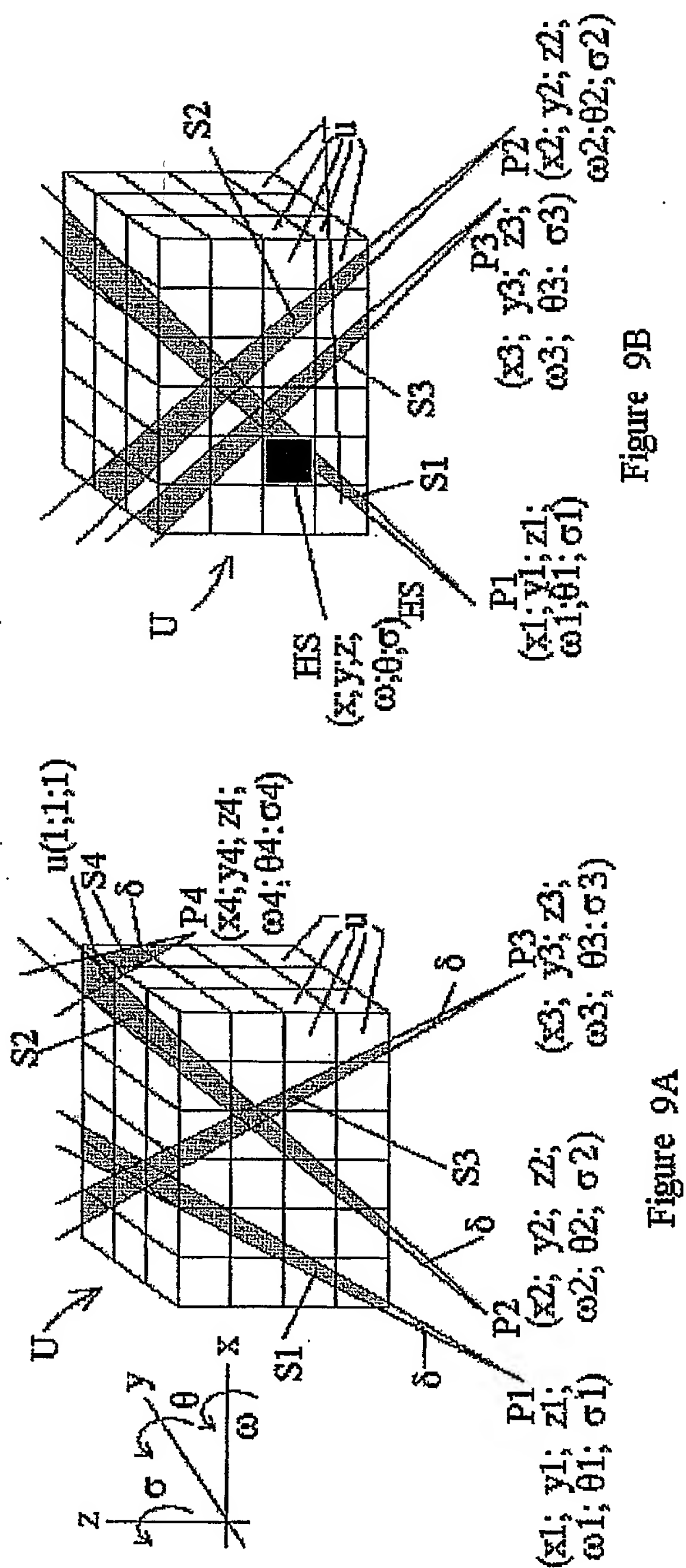


Figure 9B

Figure 9A

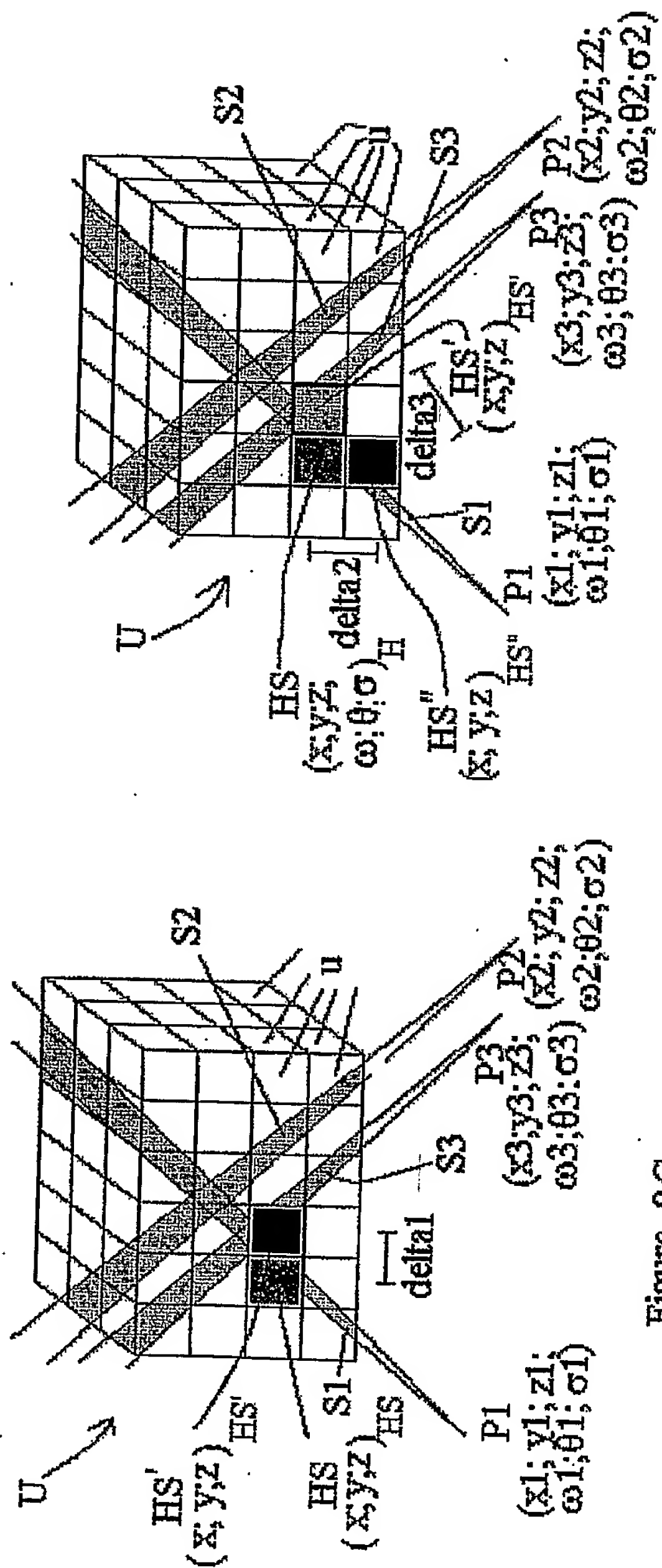


Figure 9C

Figure 9D

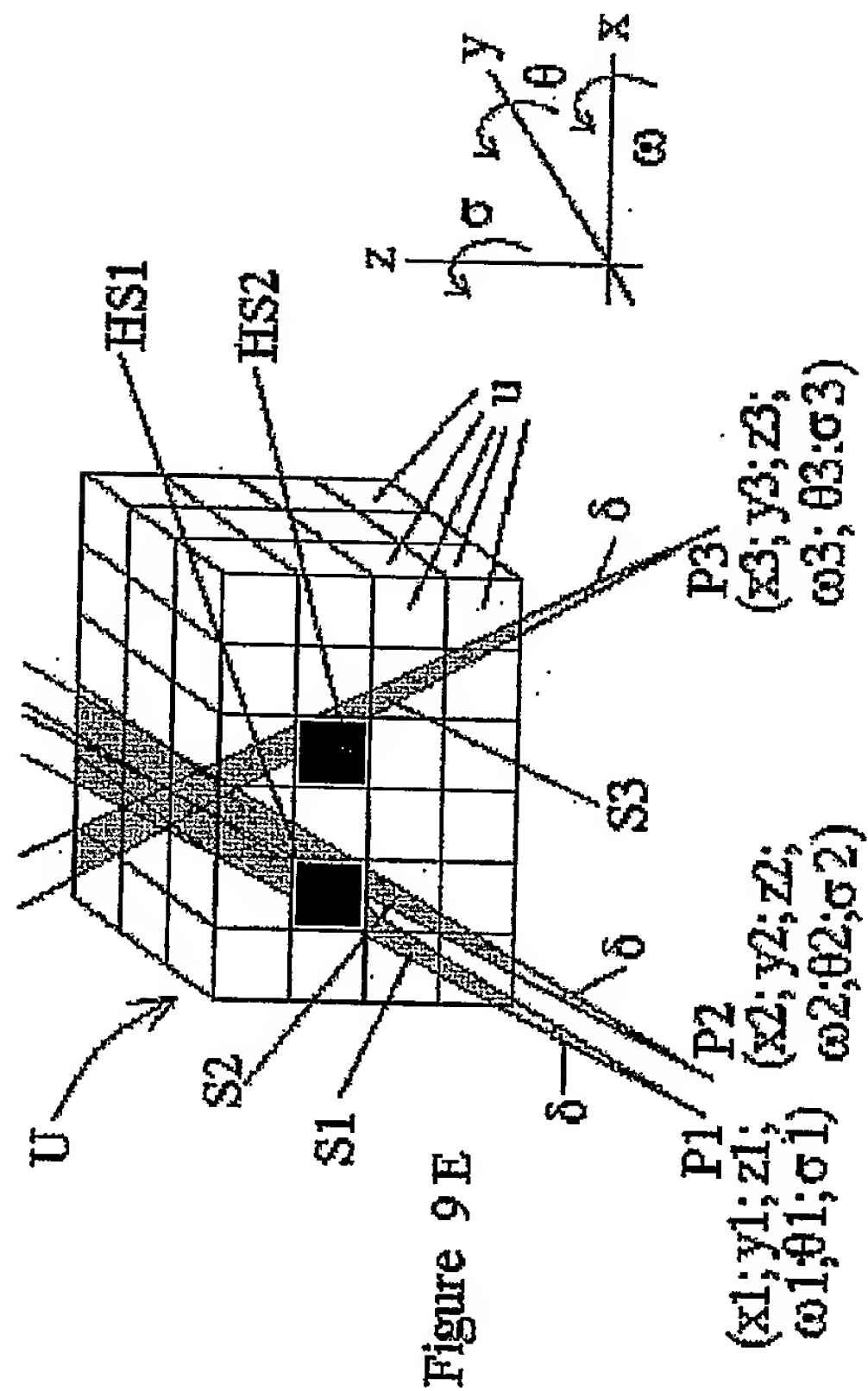
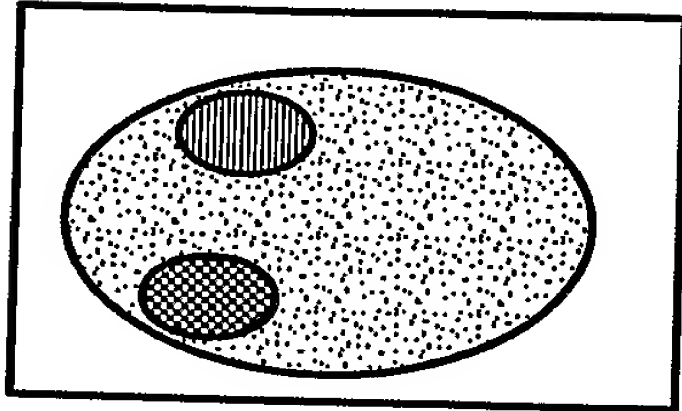


Figure 9E

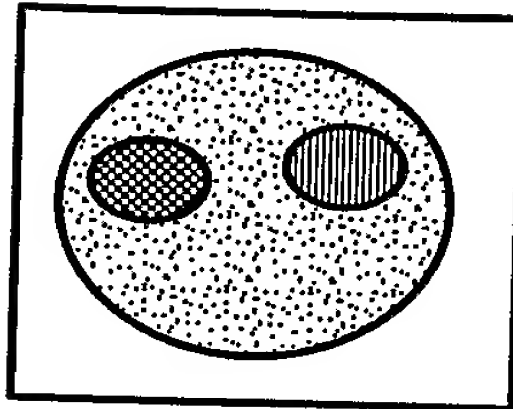
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X-Y Projection

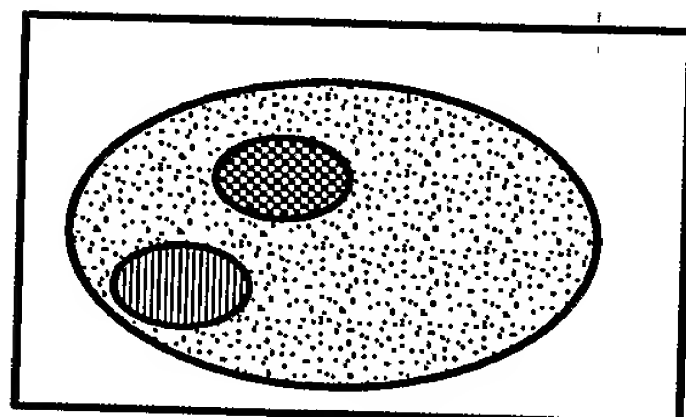
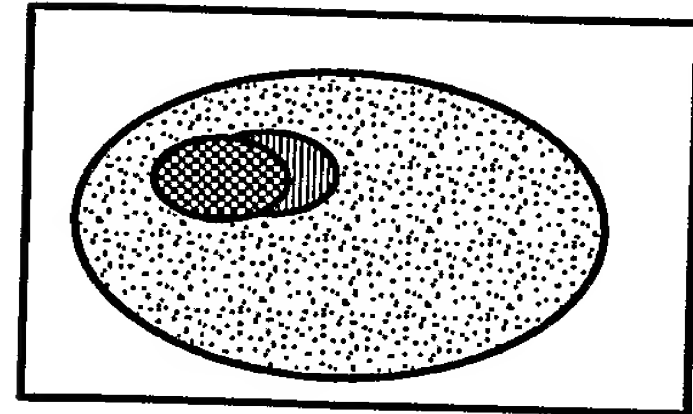


Model 1

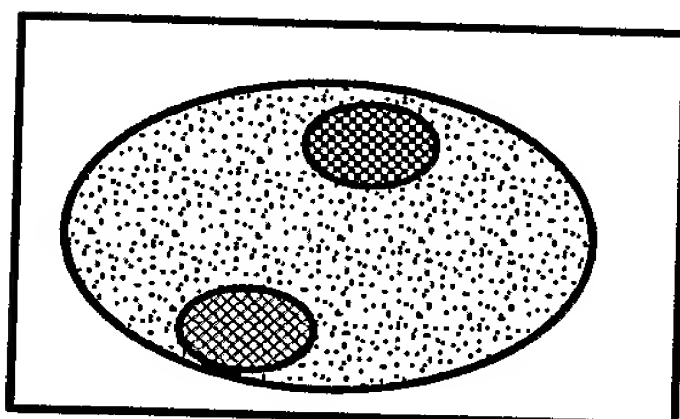
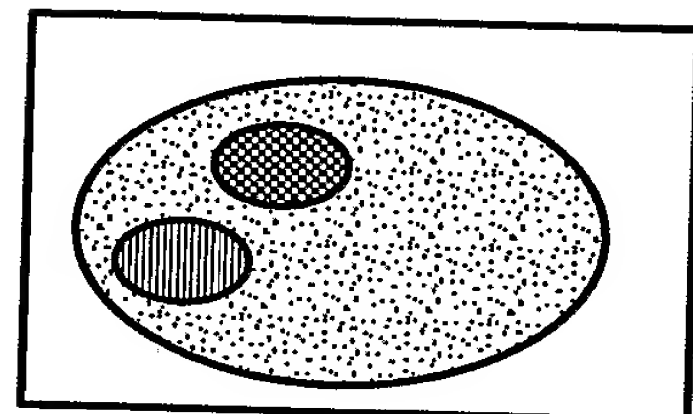
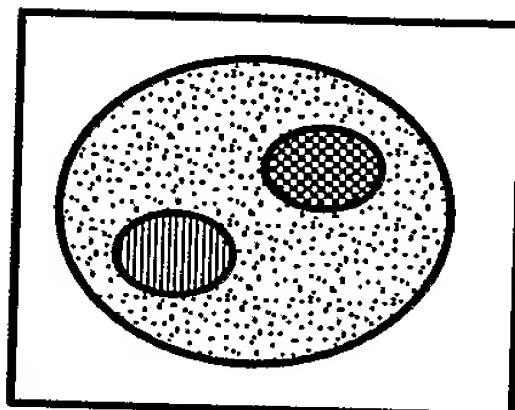
Y-Z Projection



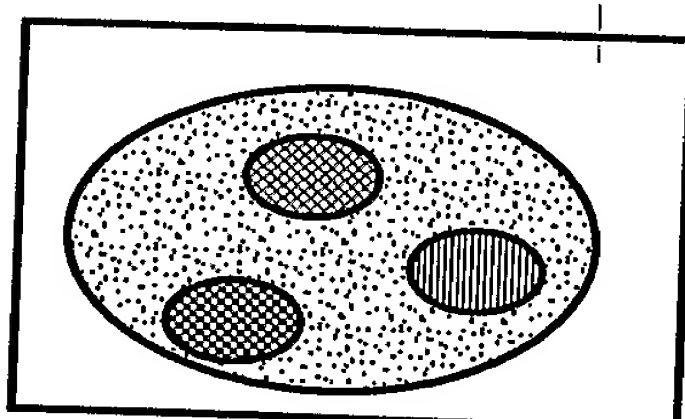
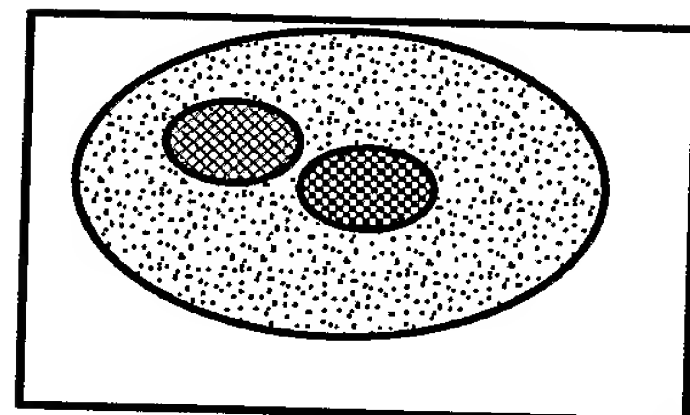
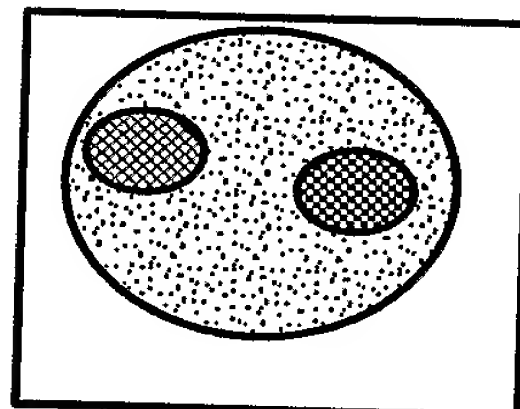
X-Z Projection



Model 2



Model 3



Model 4

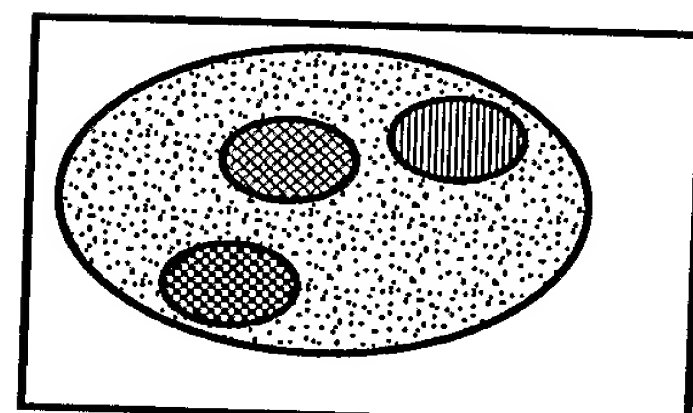
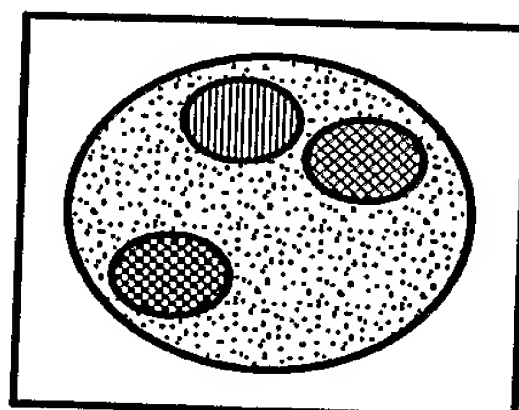
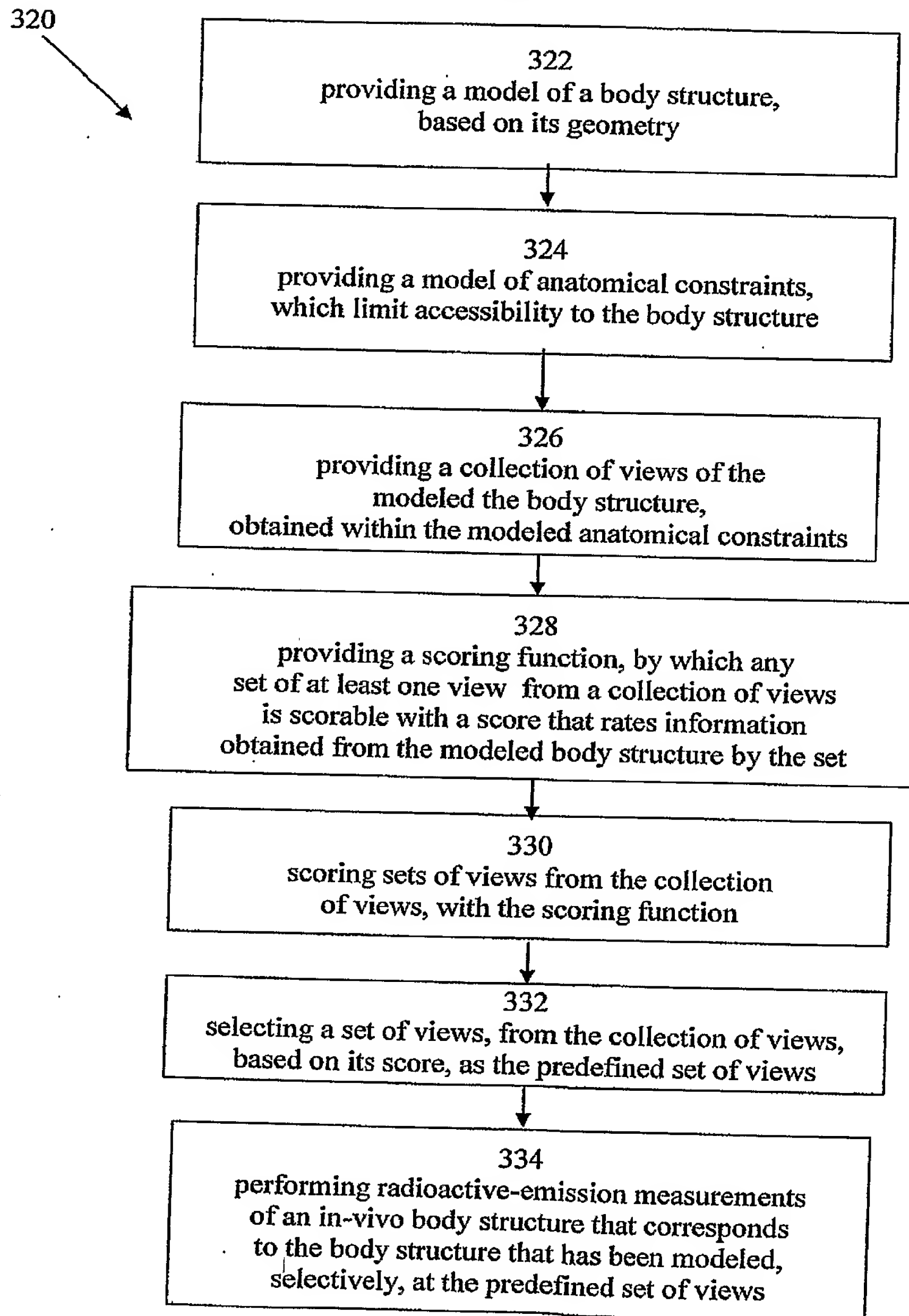


Fig. 9F

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Figure 10



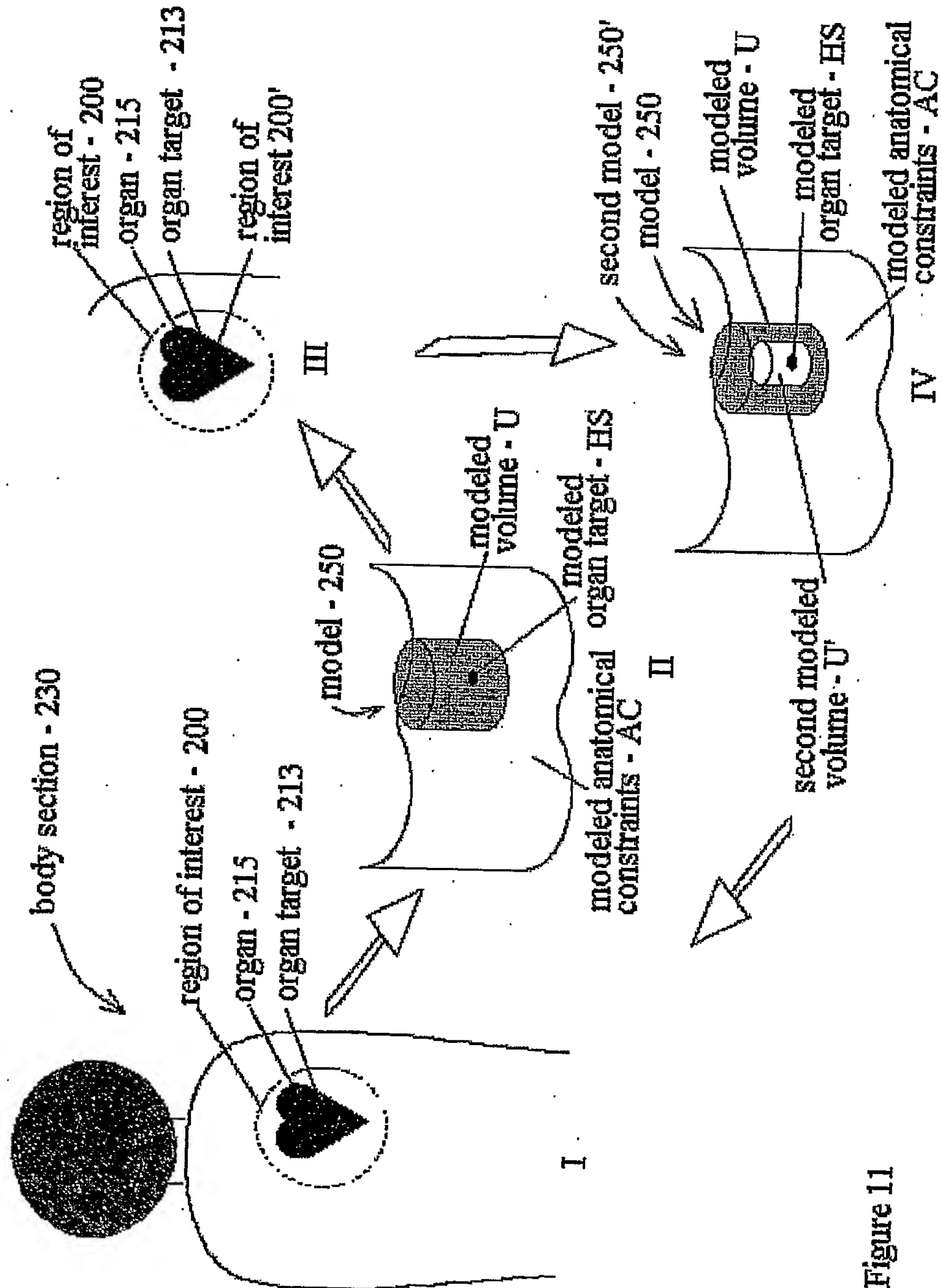
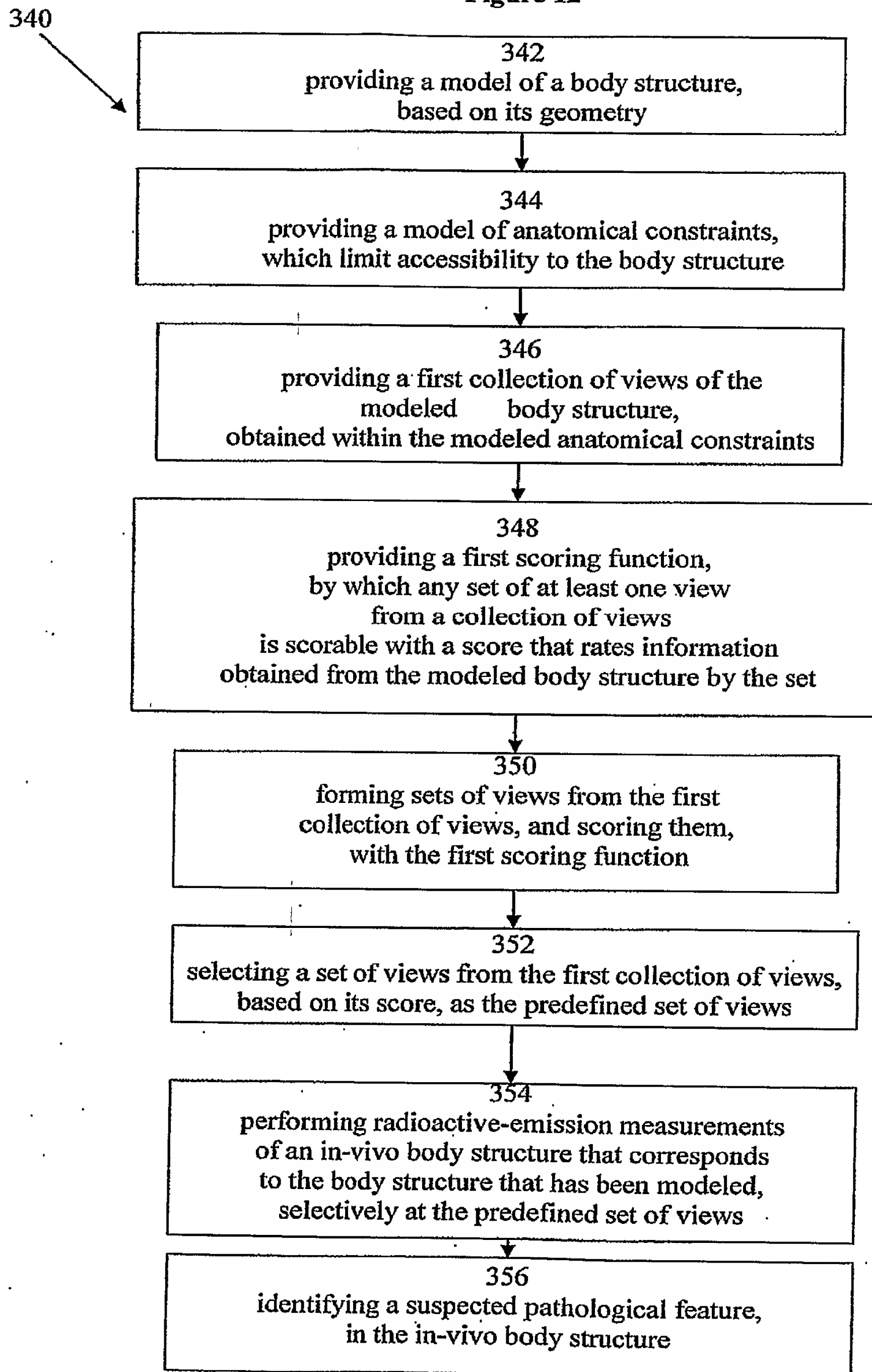


Figure 11



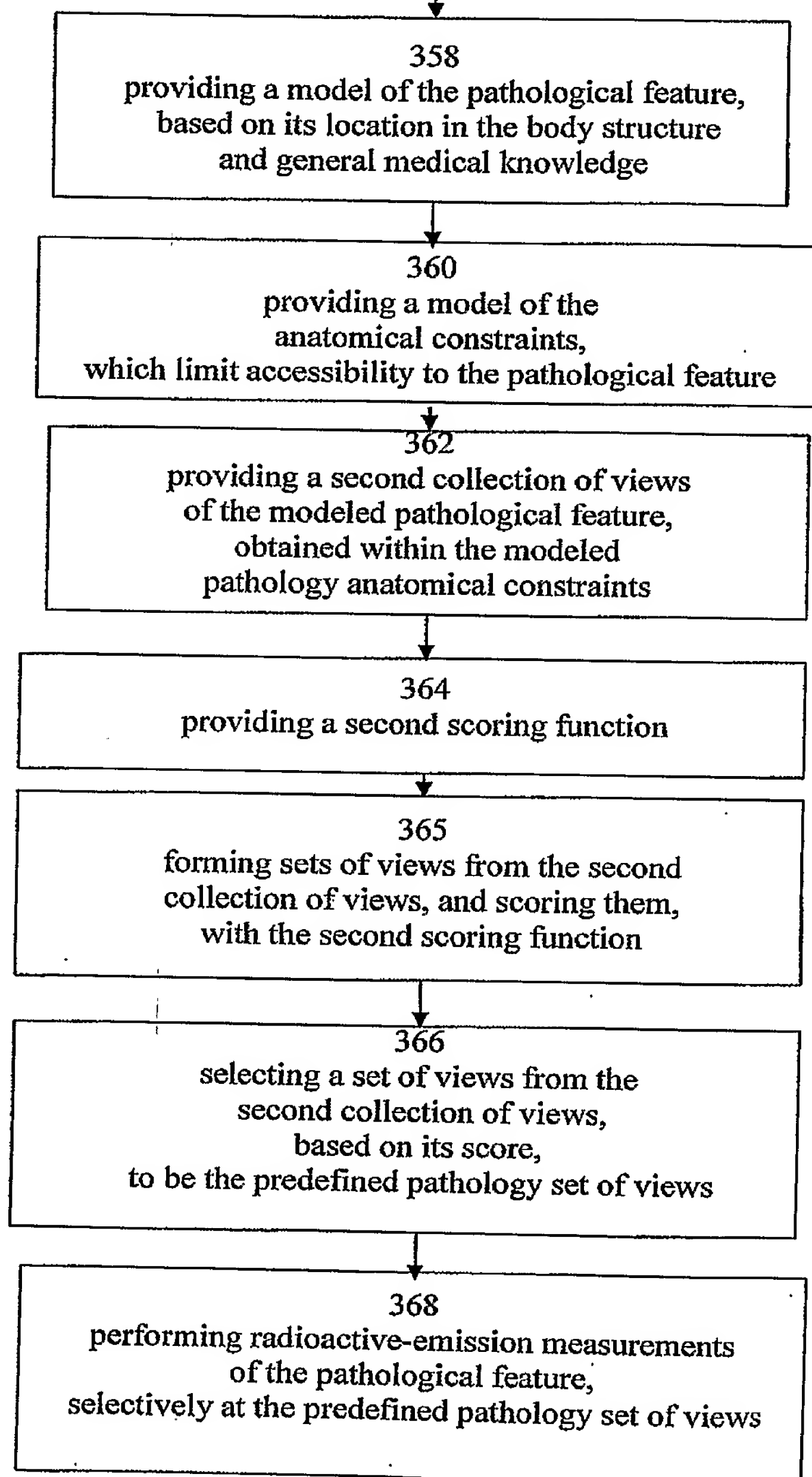
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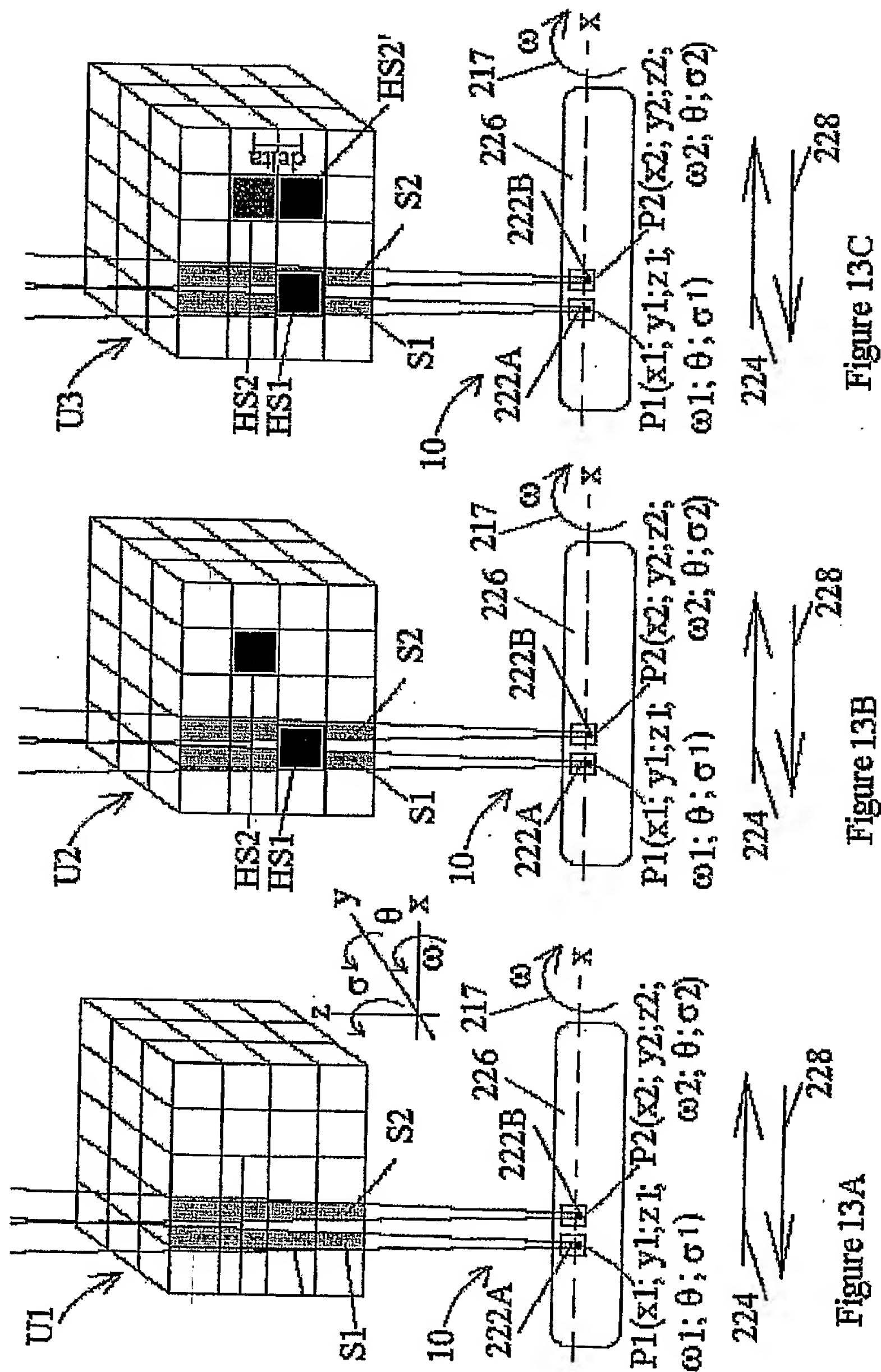
Figure 12



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Figure 12 (continued)





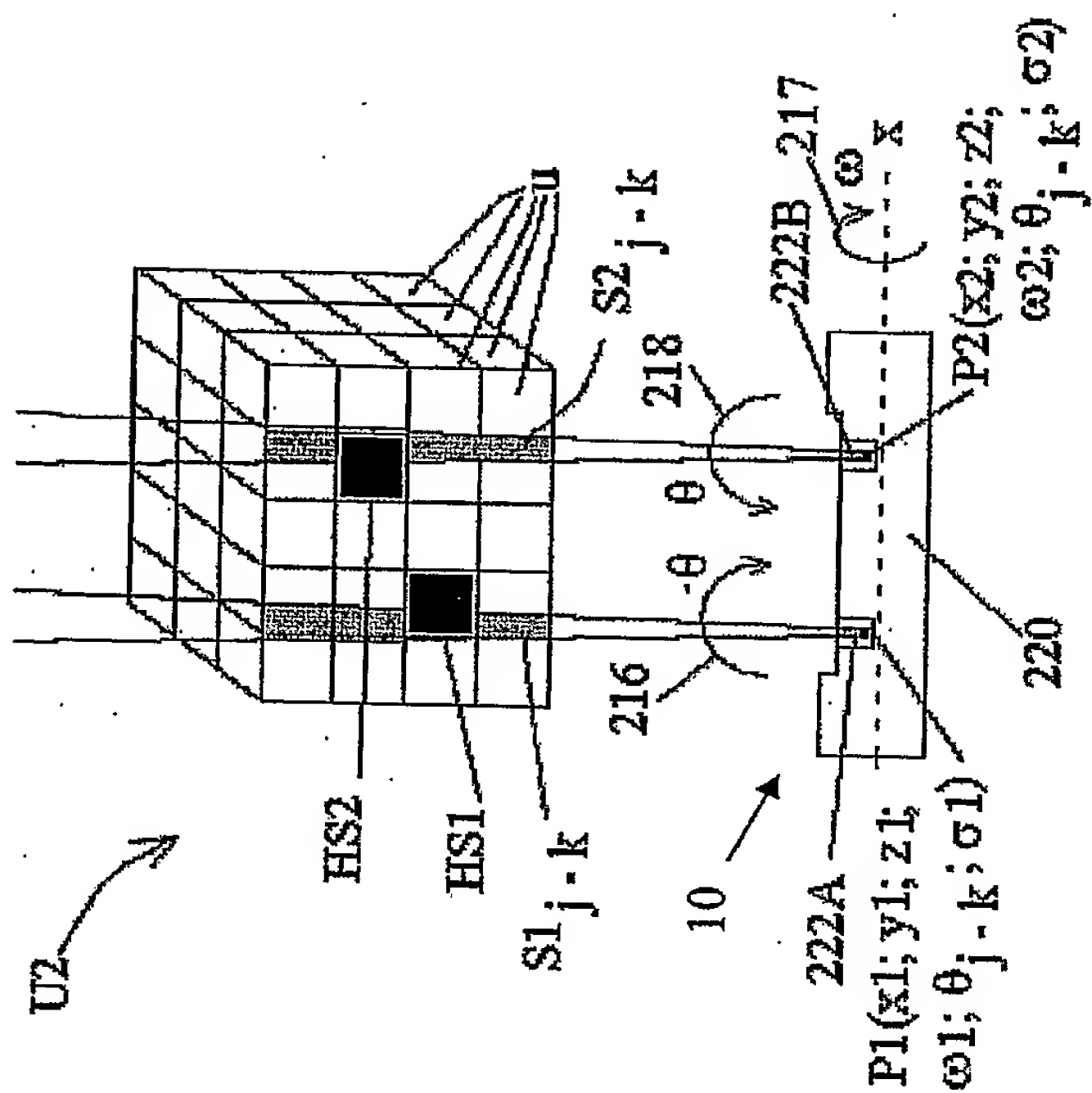


Figure 13D

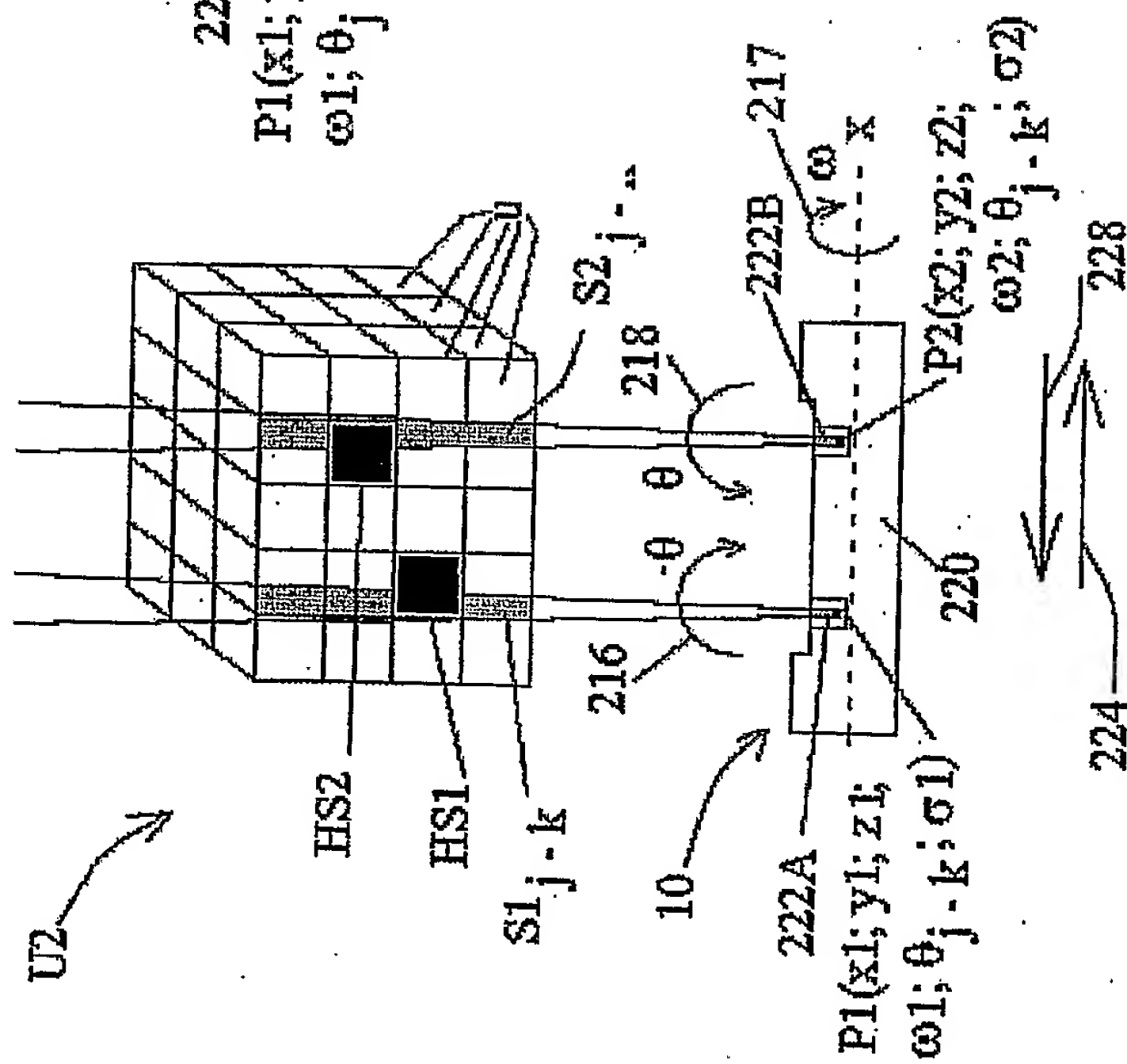
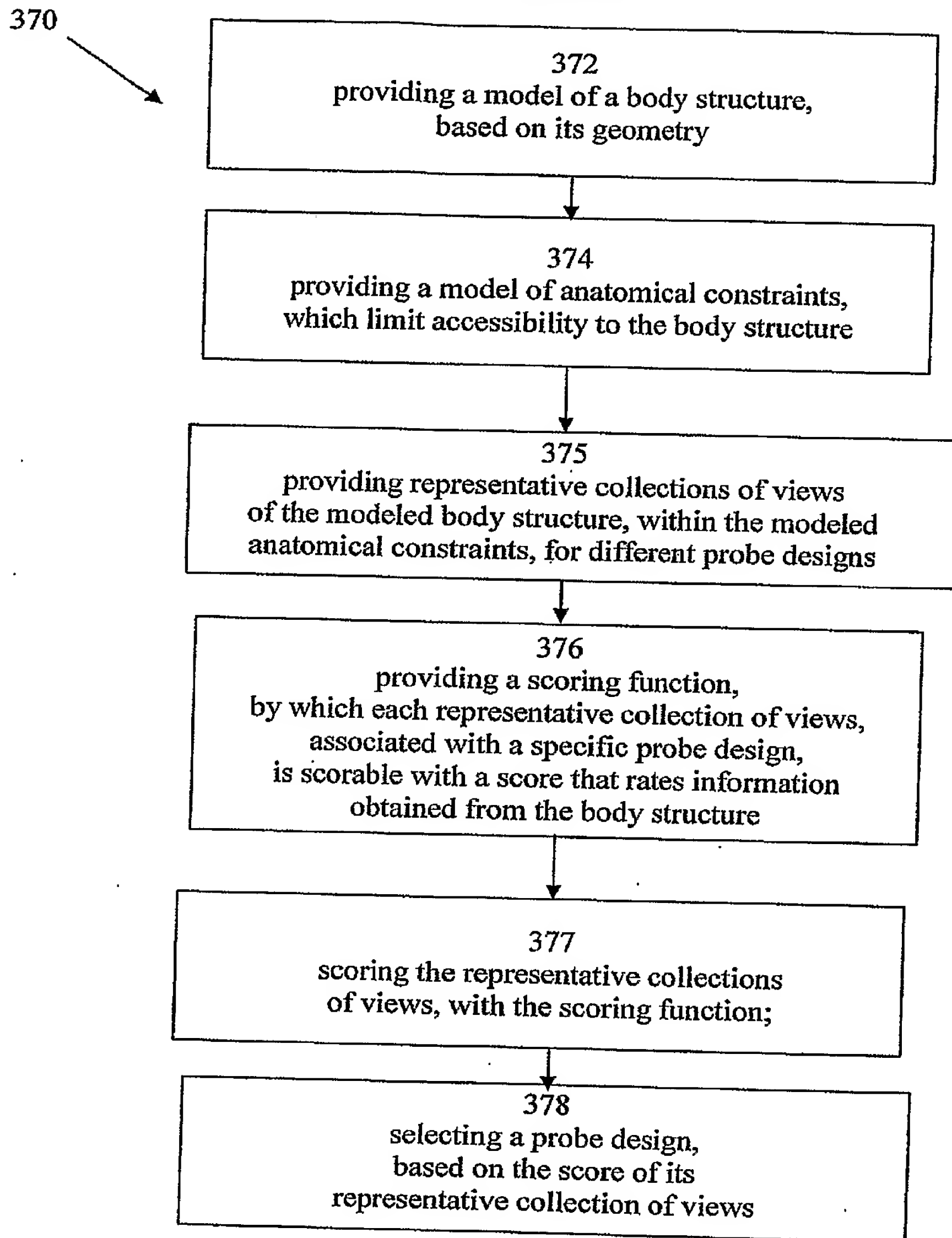


Figure 13E

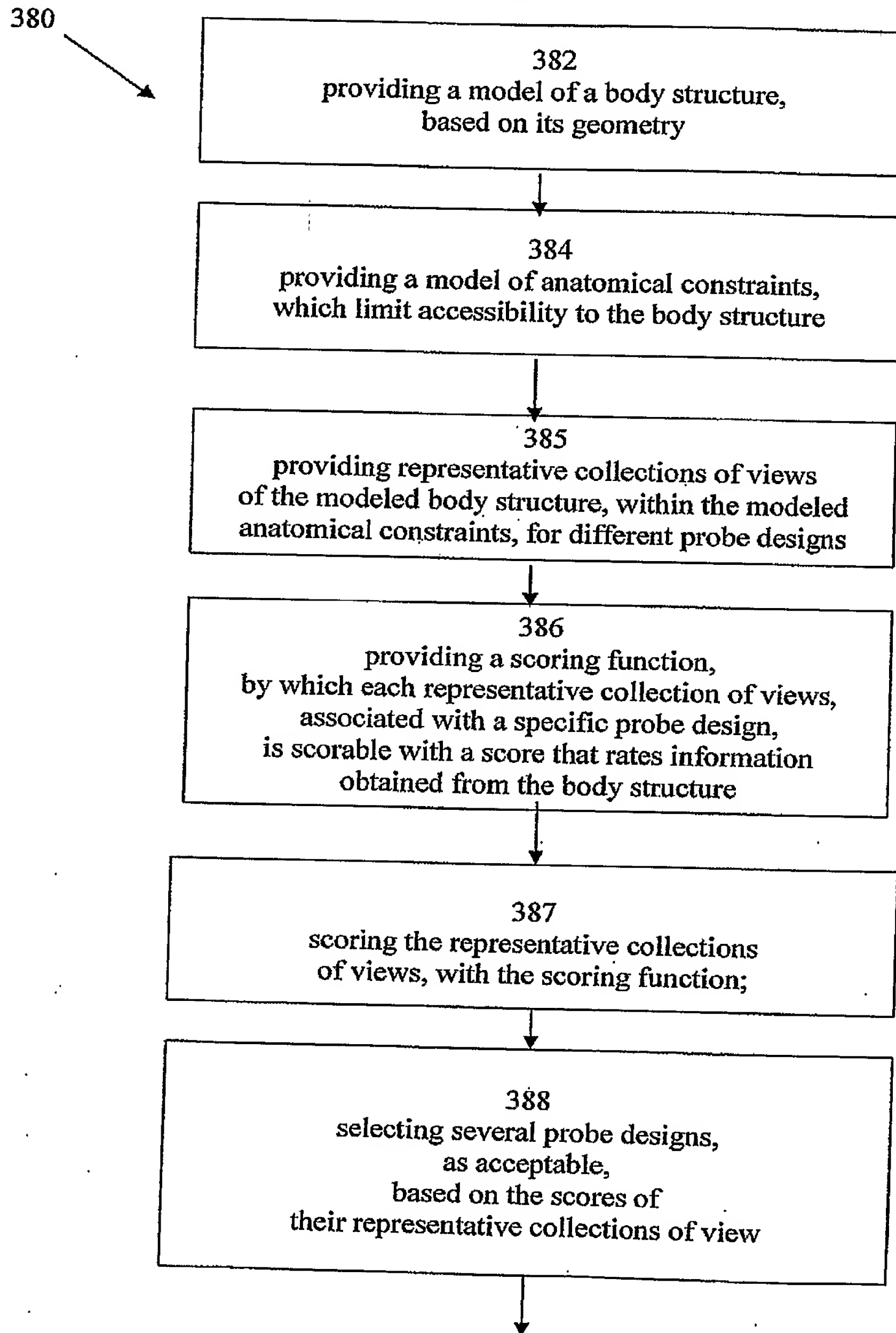
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Figure 14



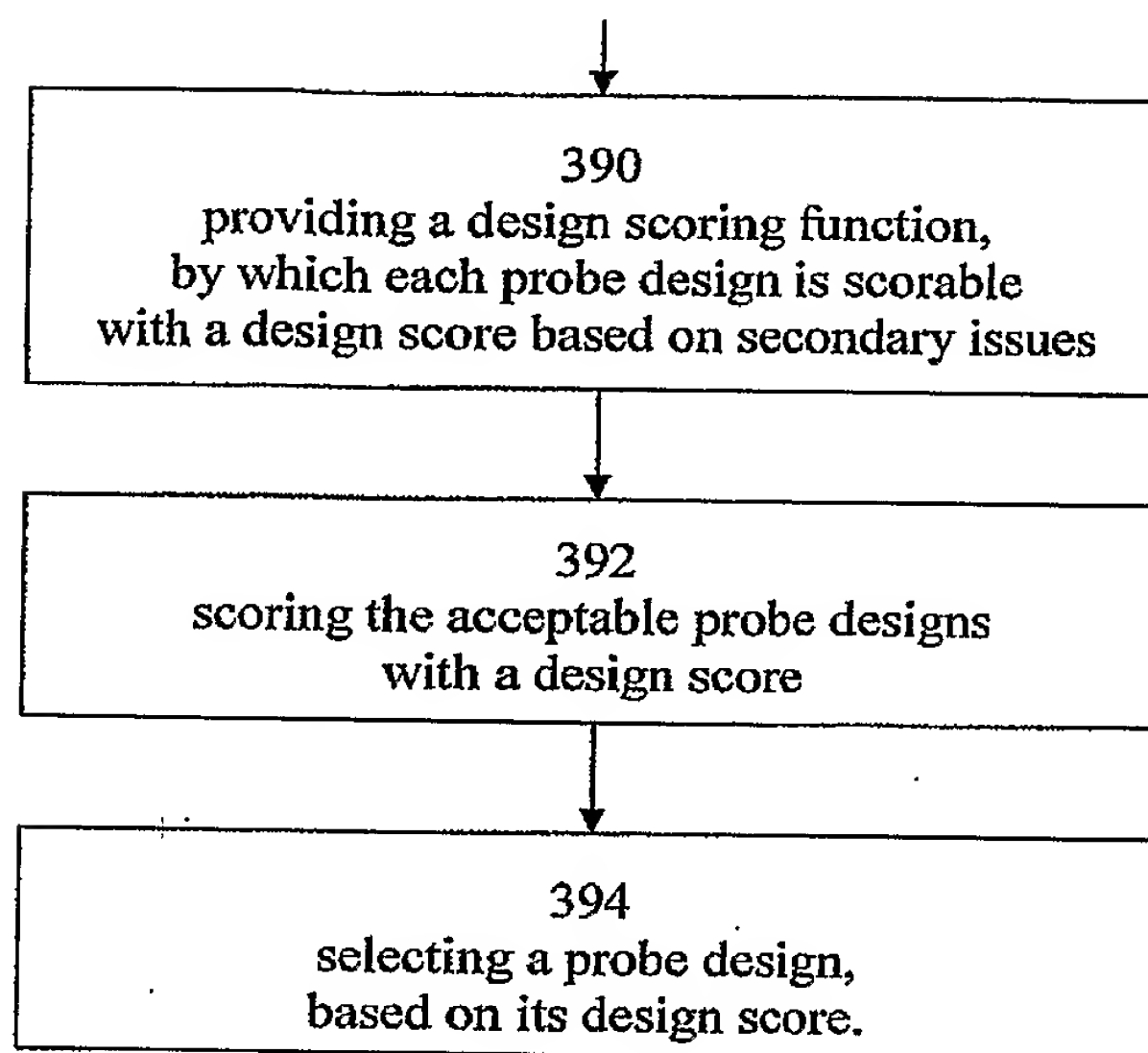
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Figure 15



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Figure 15 (continued)





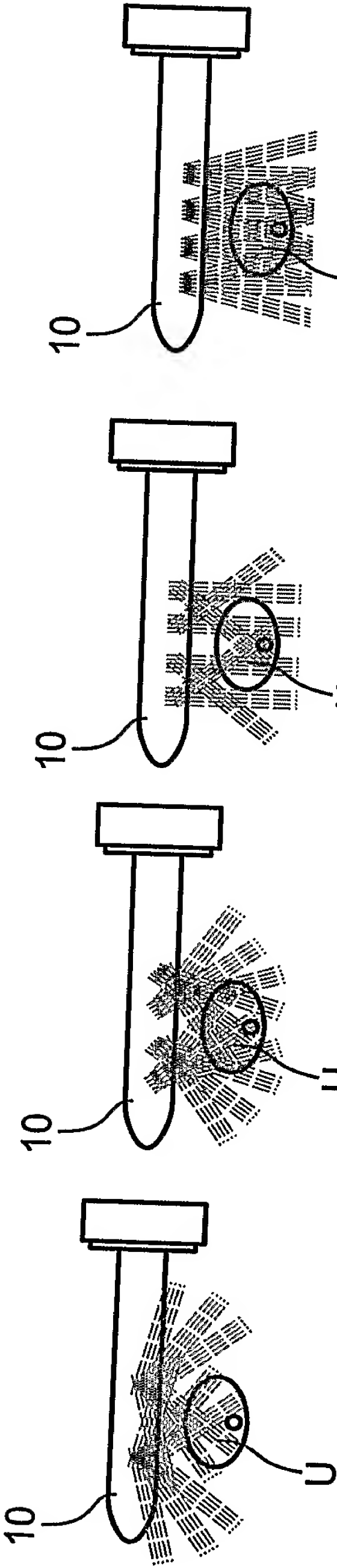


Fig. 16A

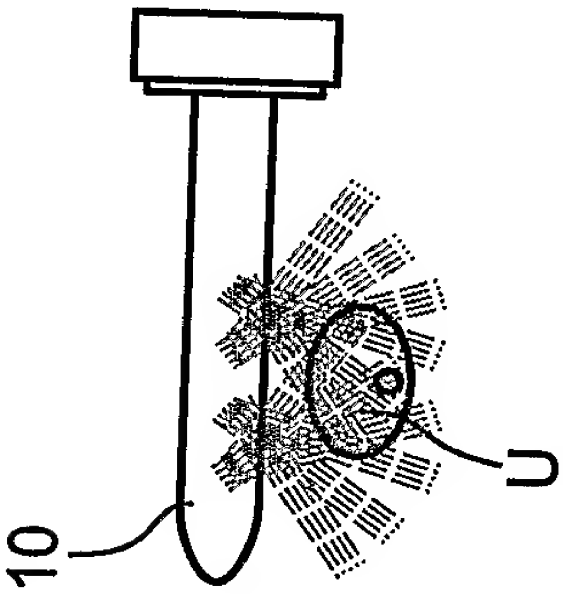


Fig. 16B

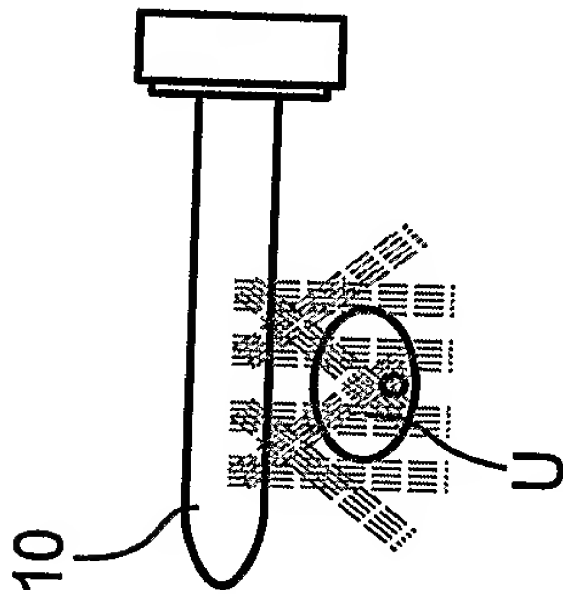


Fig. 16C

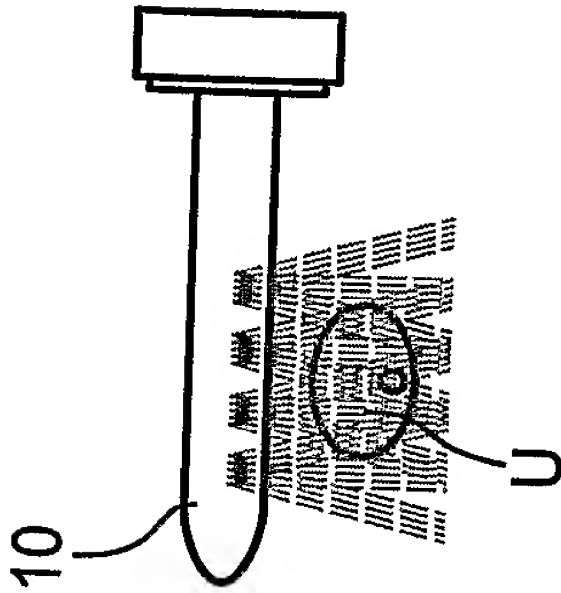


Fig. 16D

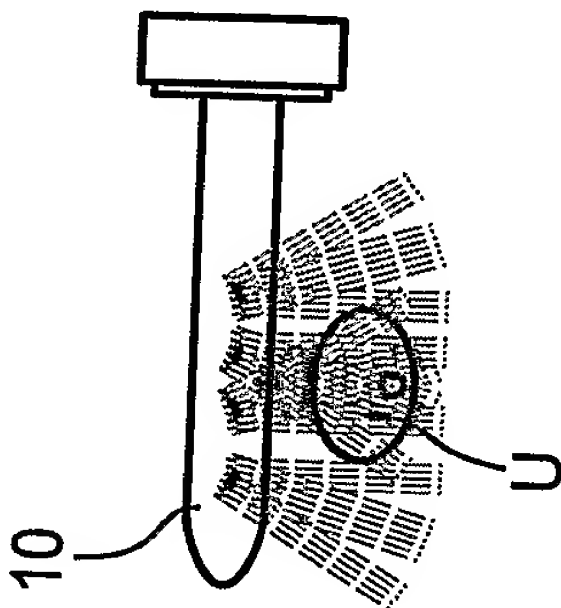


Fig. 16E

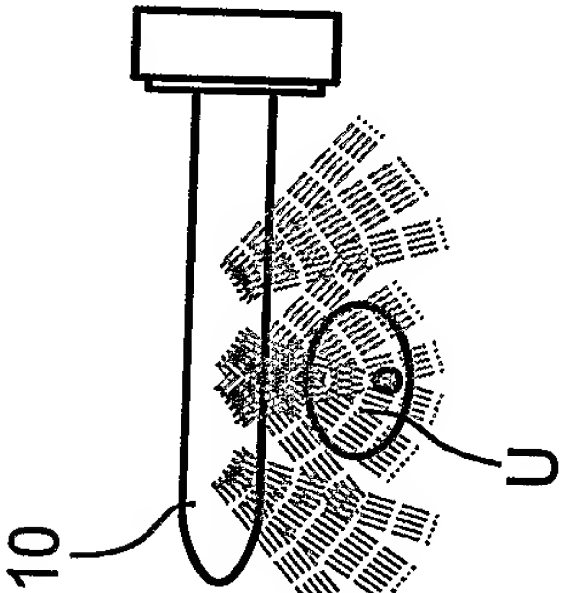


Fig. 16F

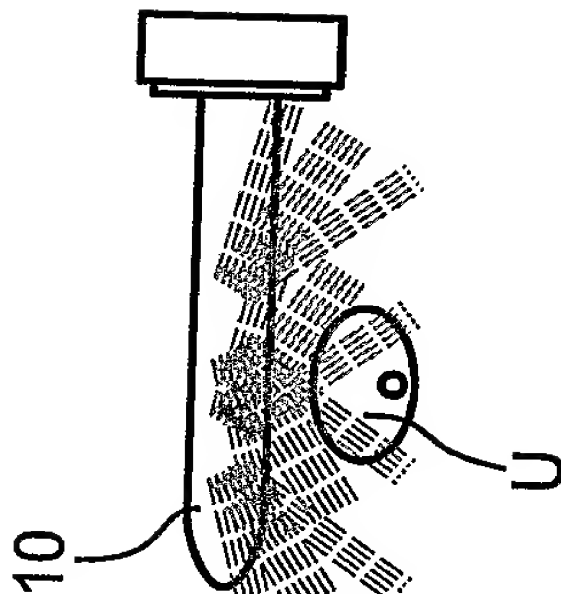


Fig. 16G

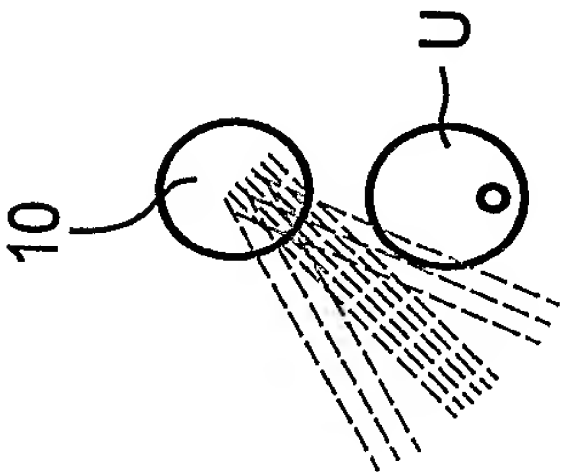


Fig. 16H

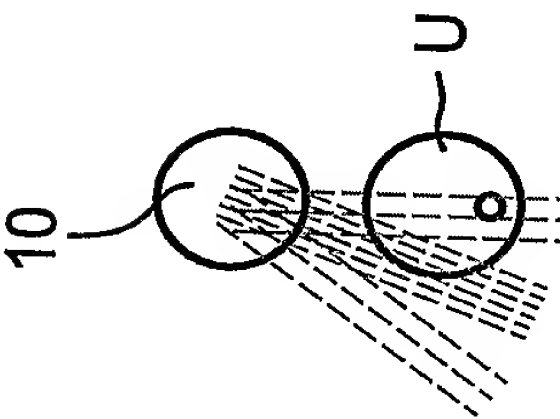


Fig. 16I

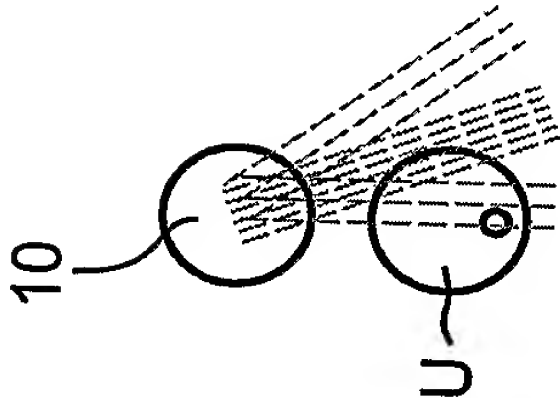


Fig. 16J

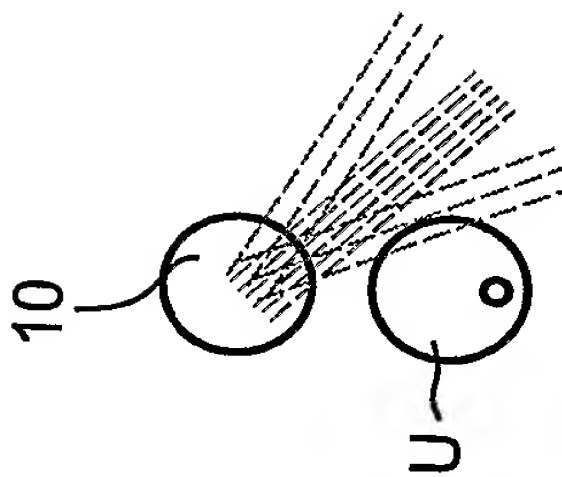


Fig. 16K

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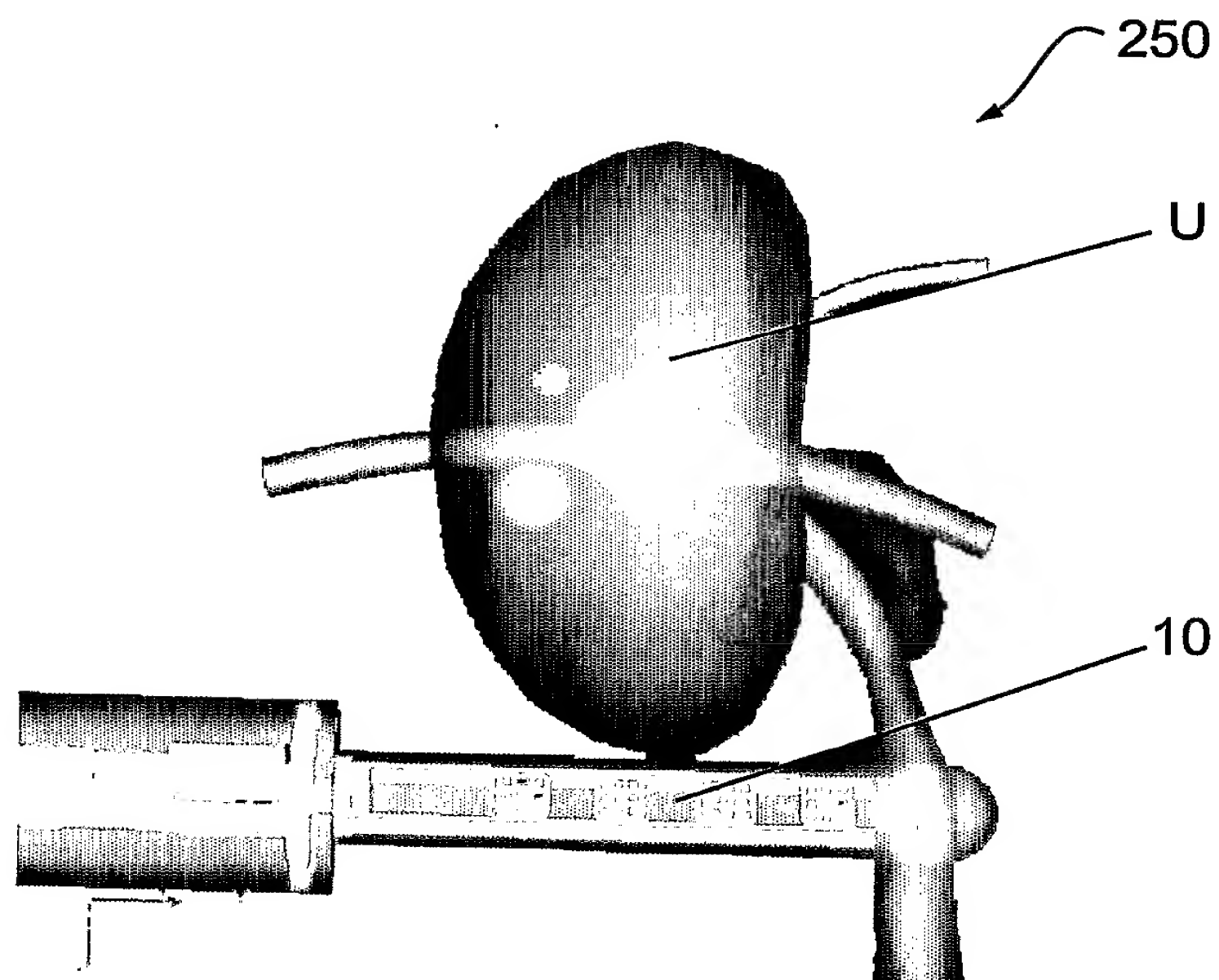


Fig. 16L

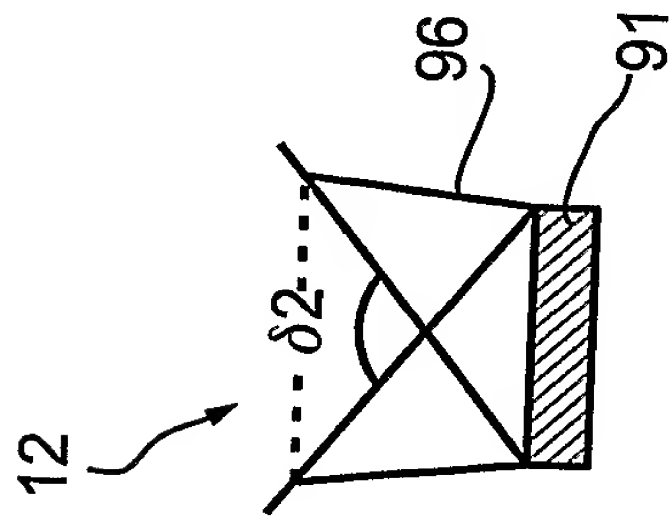


Fig. 17c

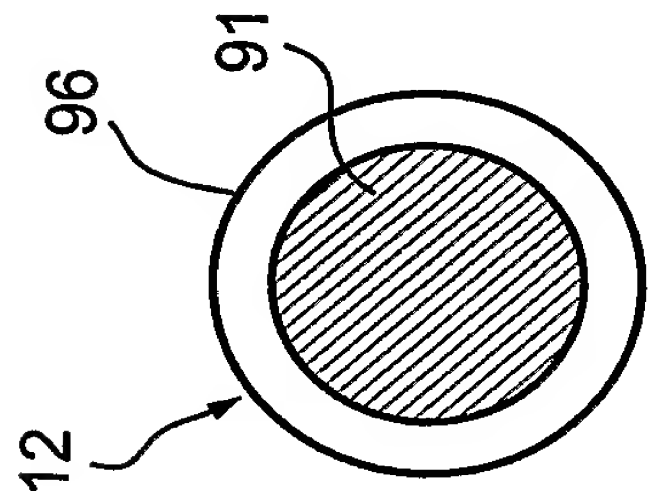


Fig. 17d

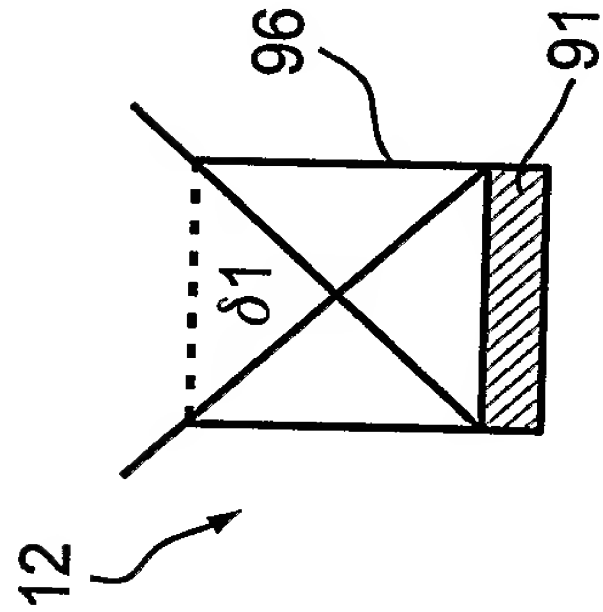


Fig. 17a

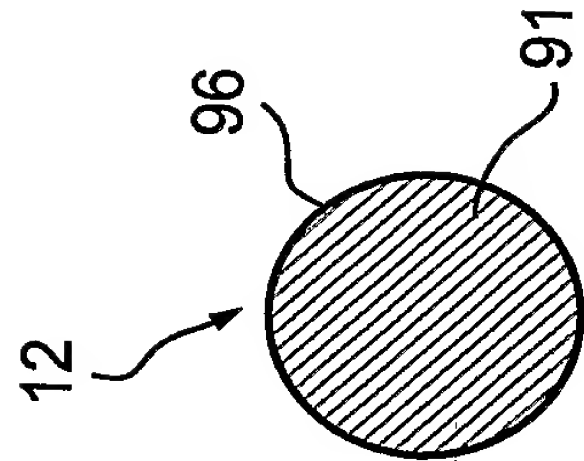


Fig. 17b

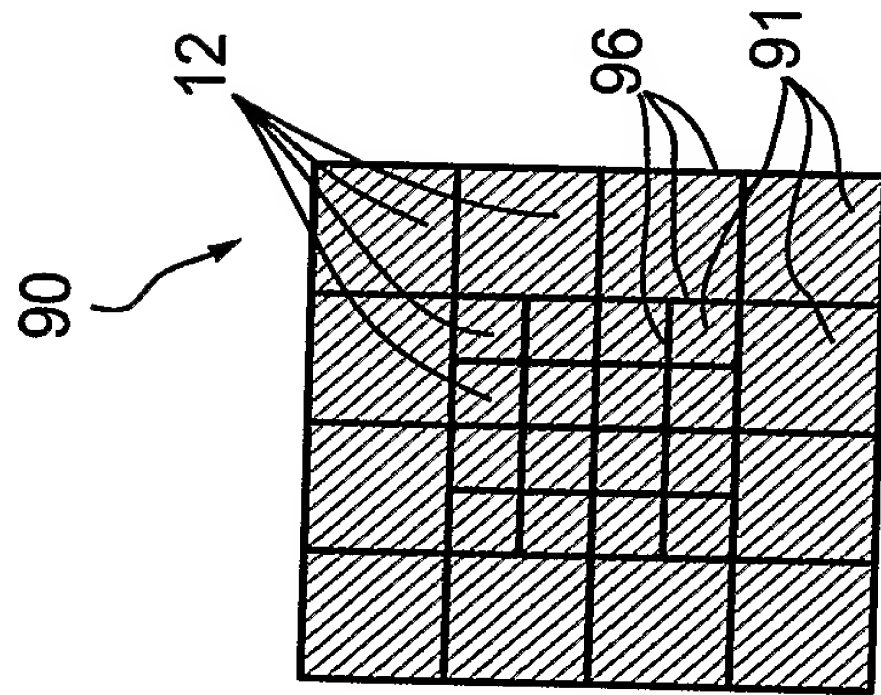


Fig. 17h

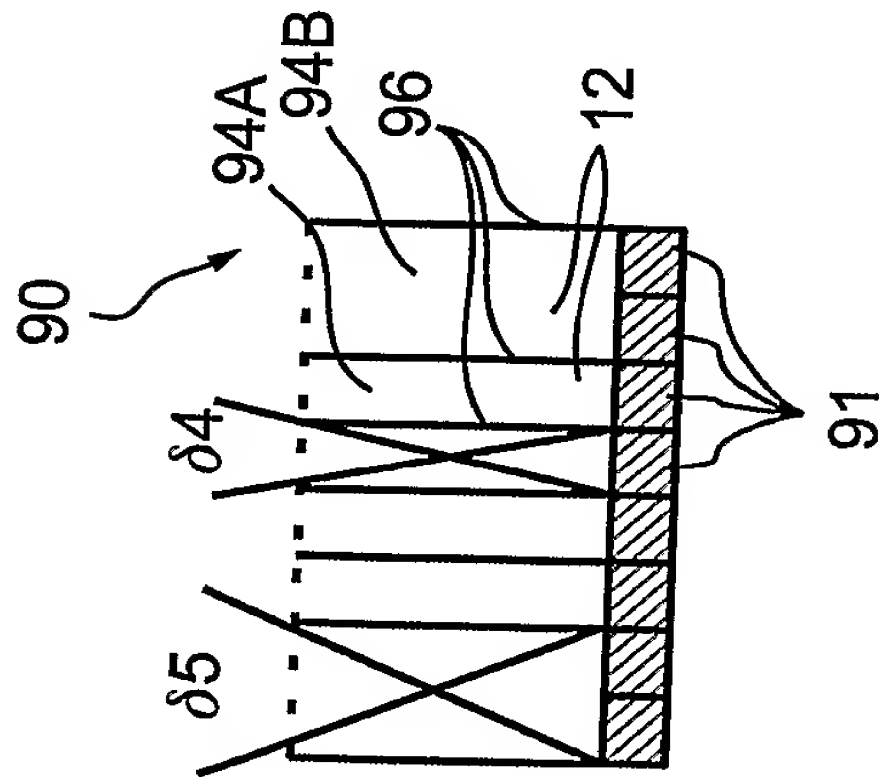


Fig. 17g

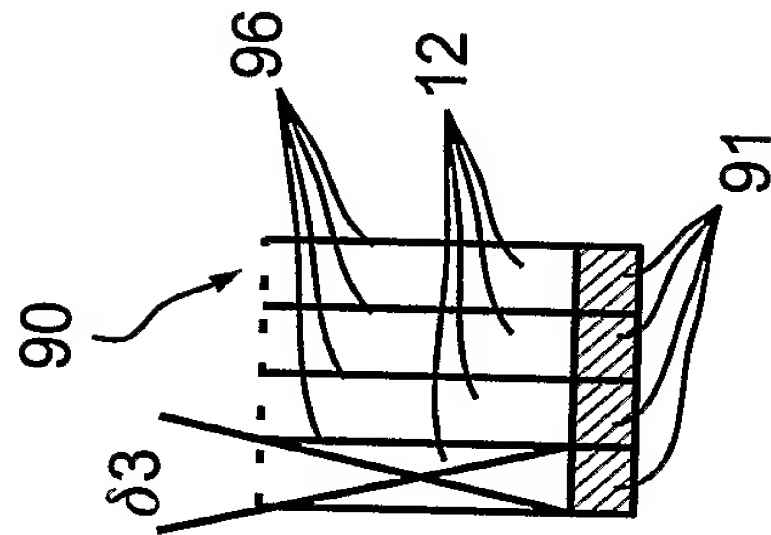


Fig. 17e

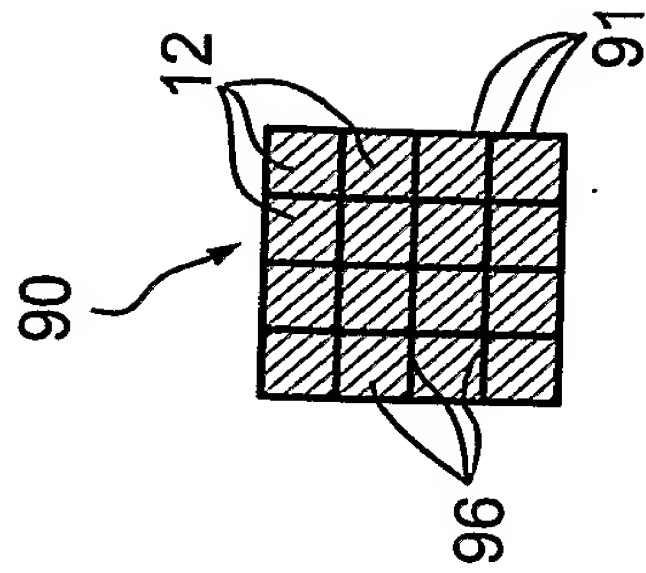
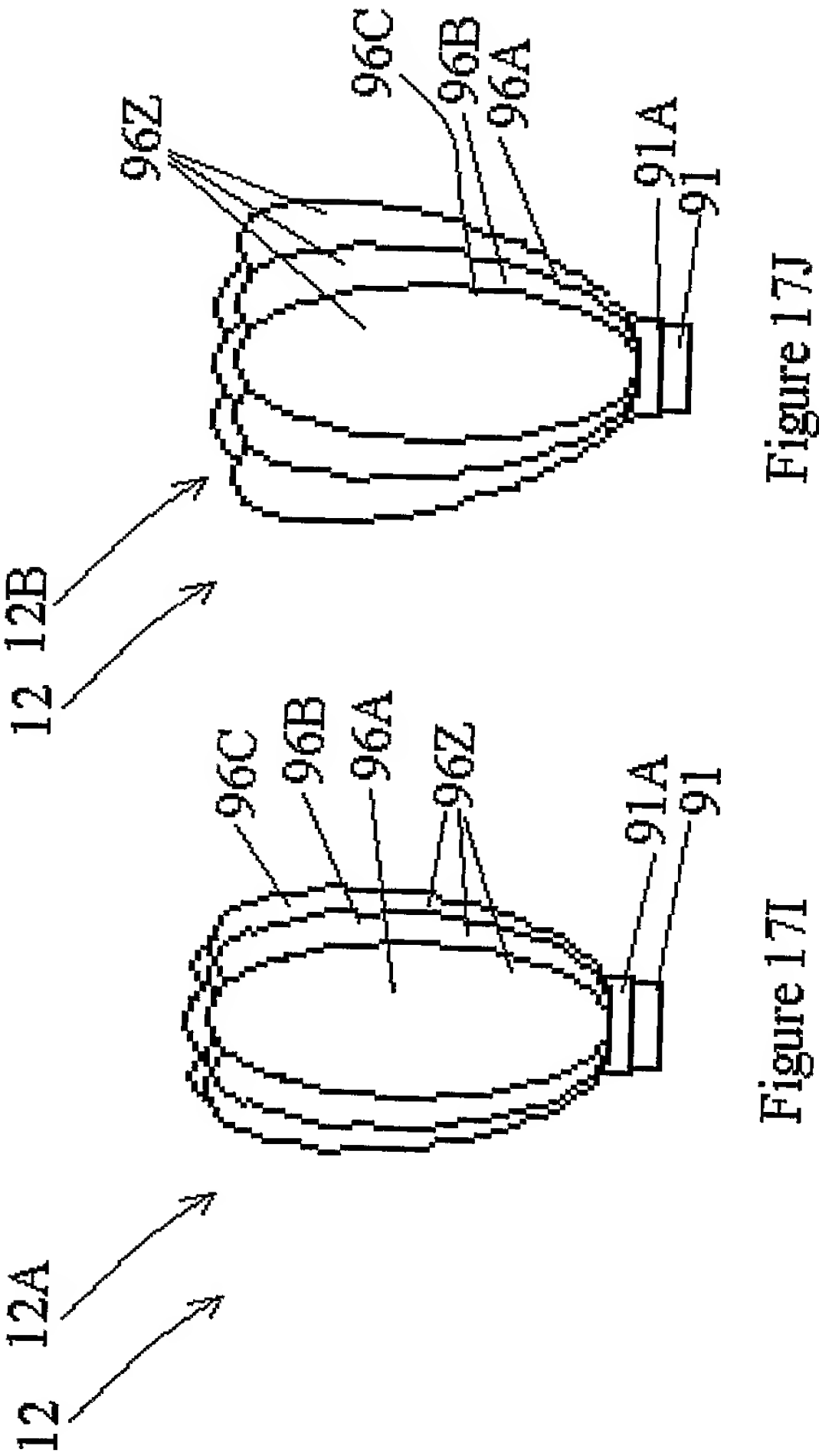
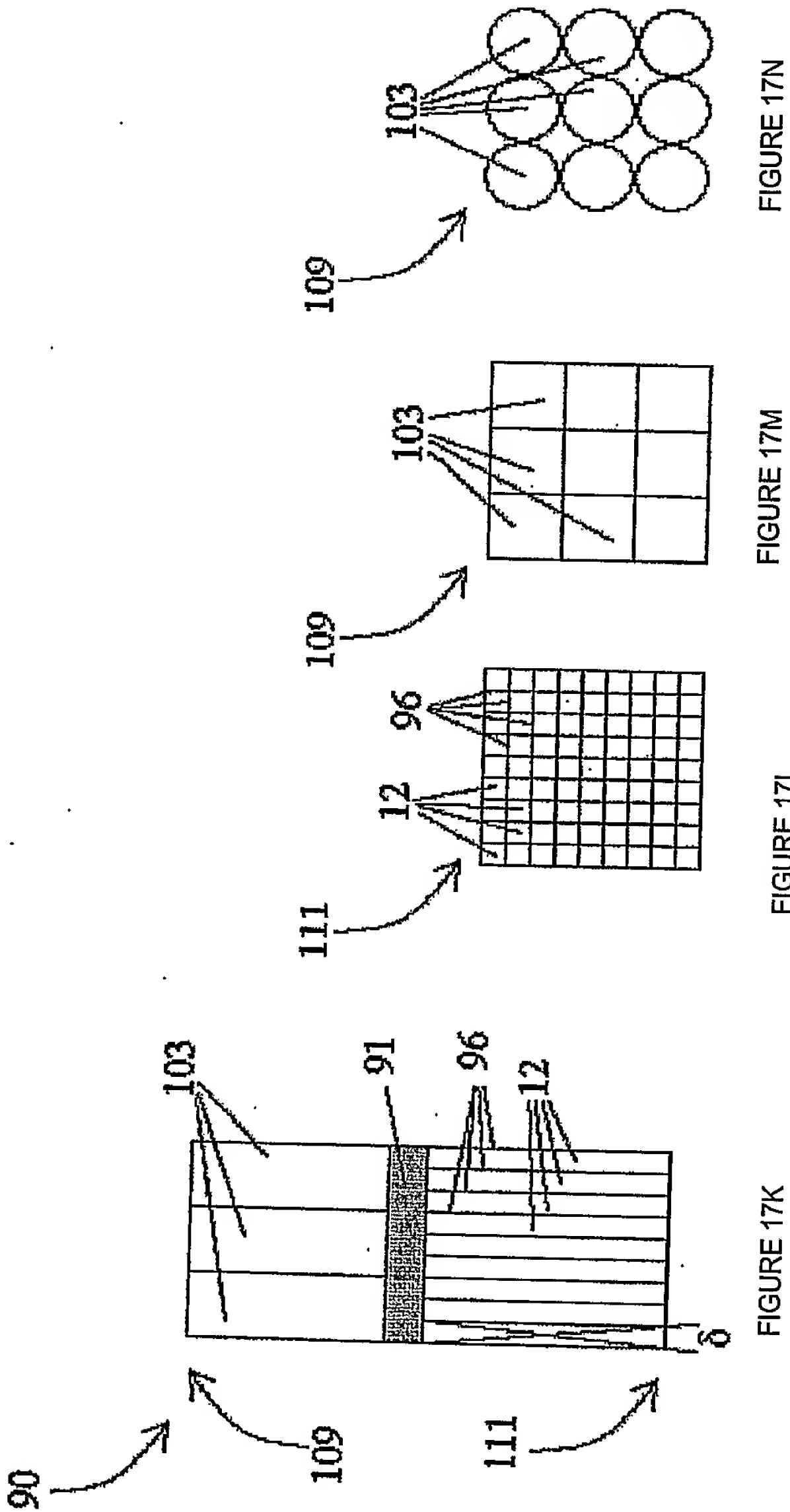
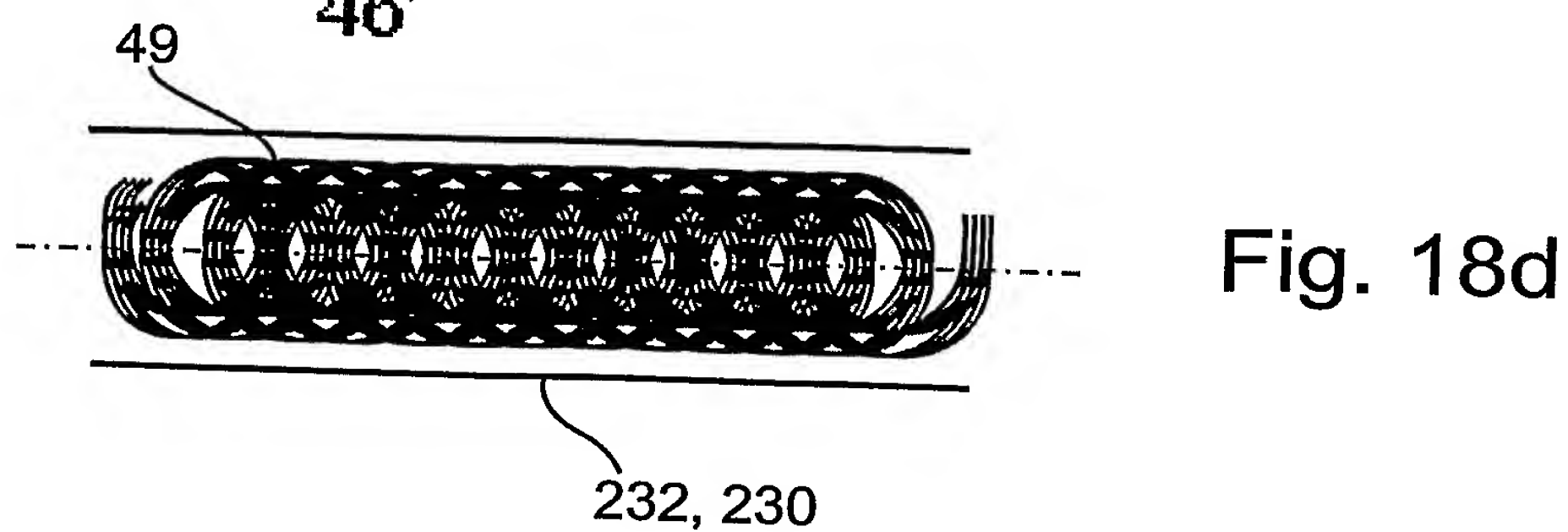
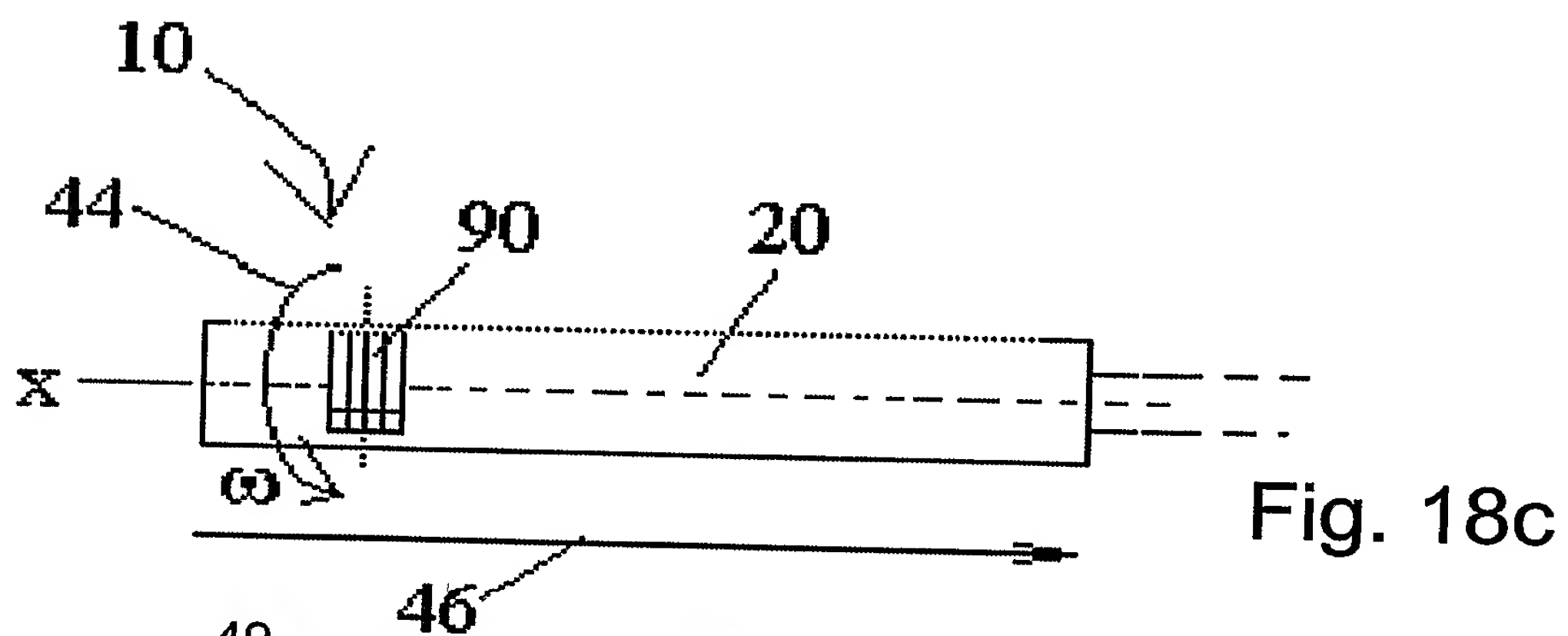
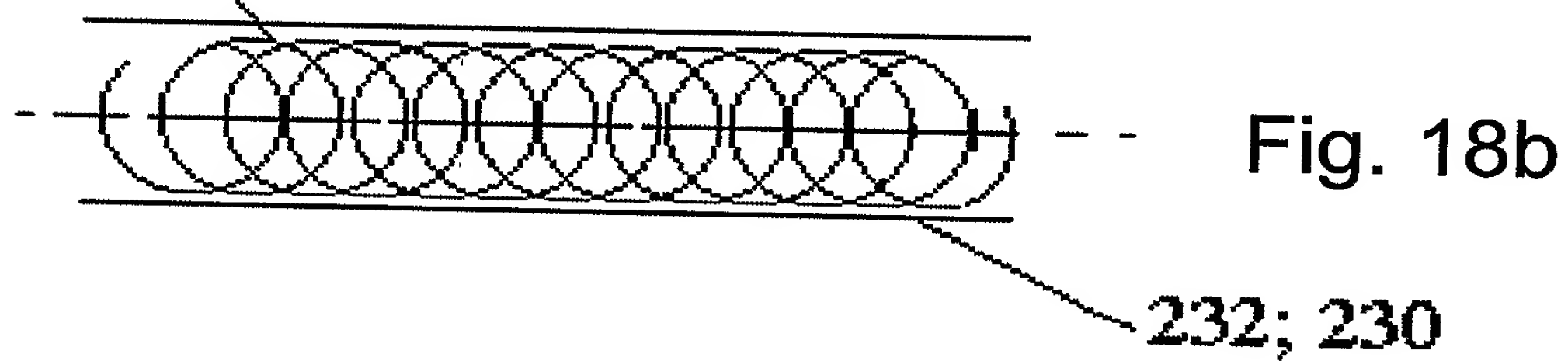
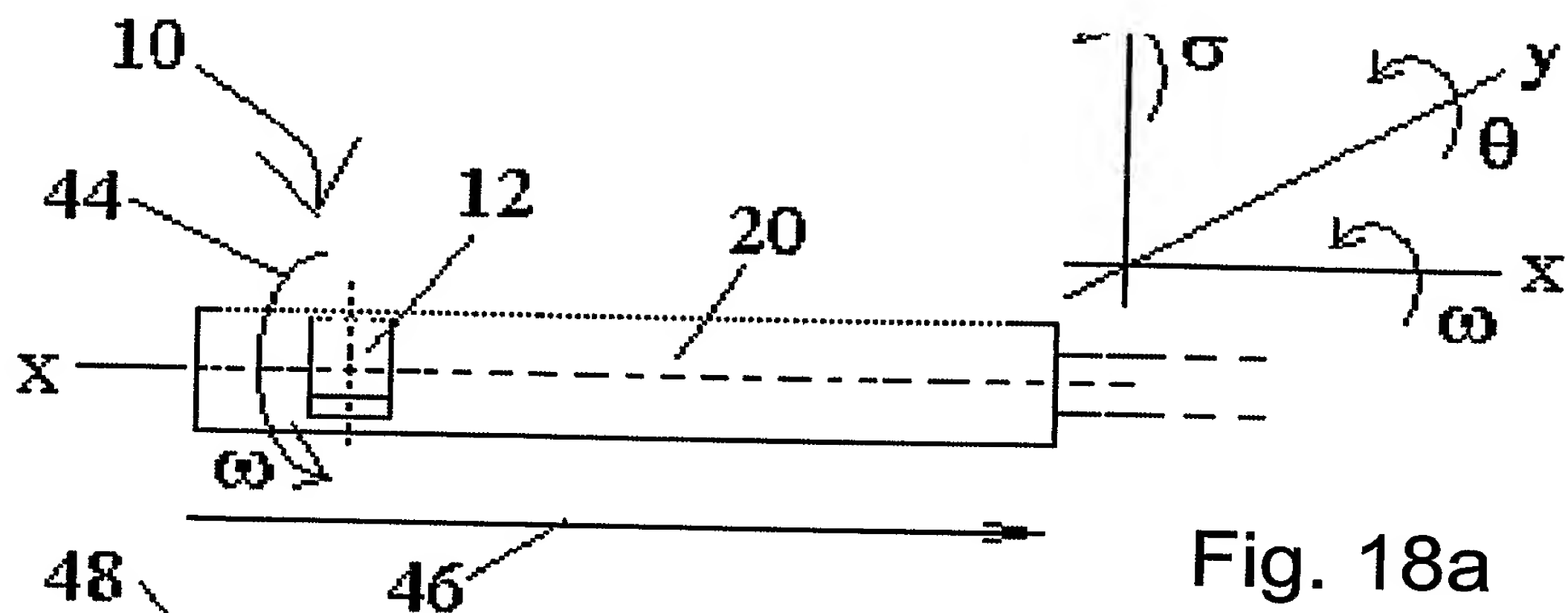


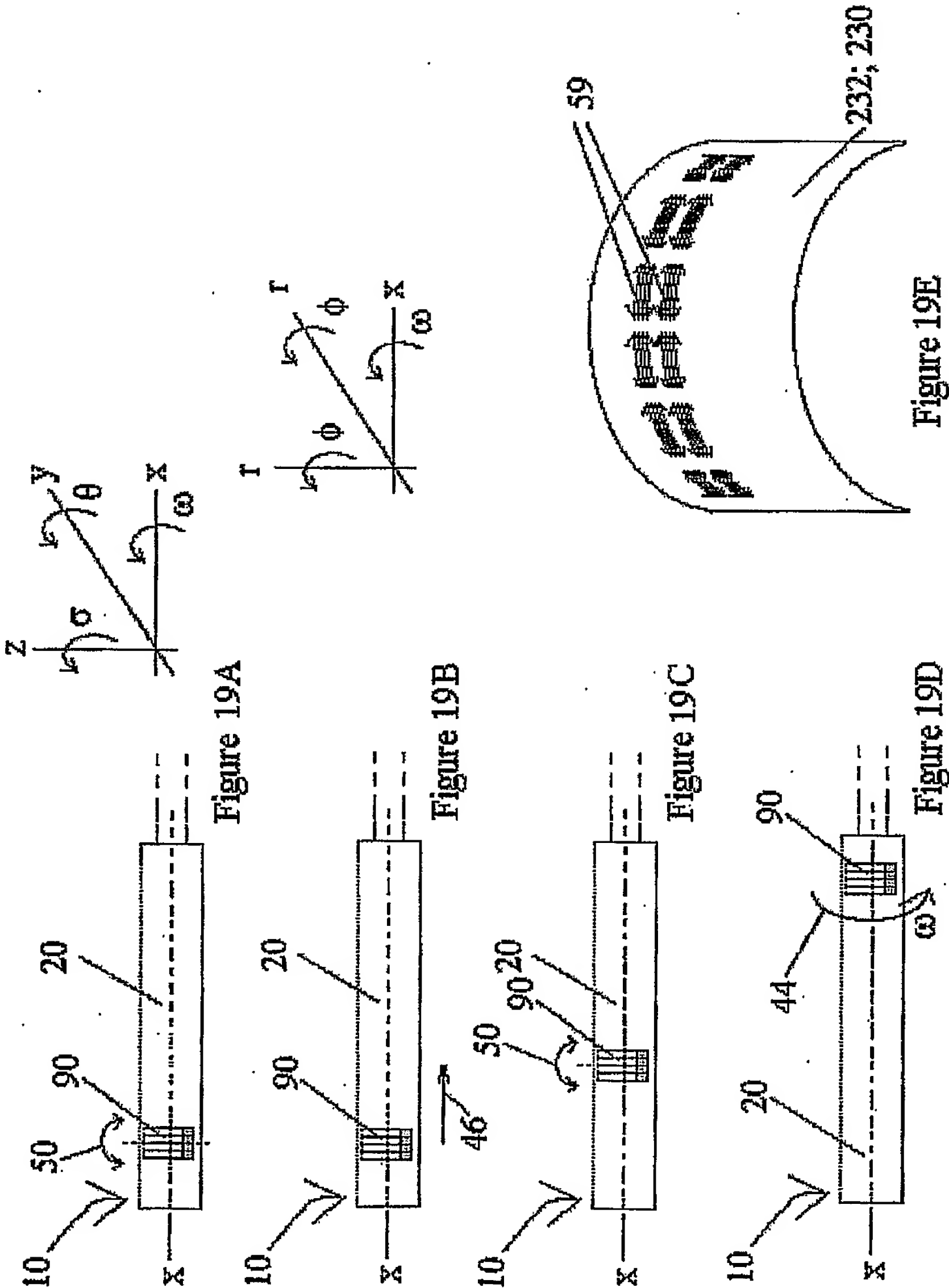
Fig. 17f



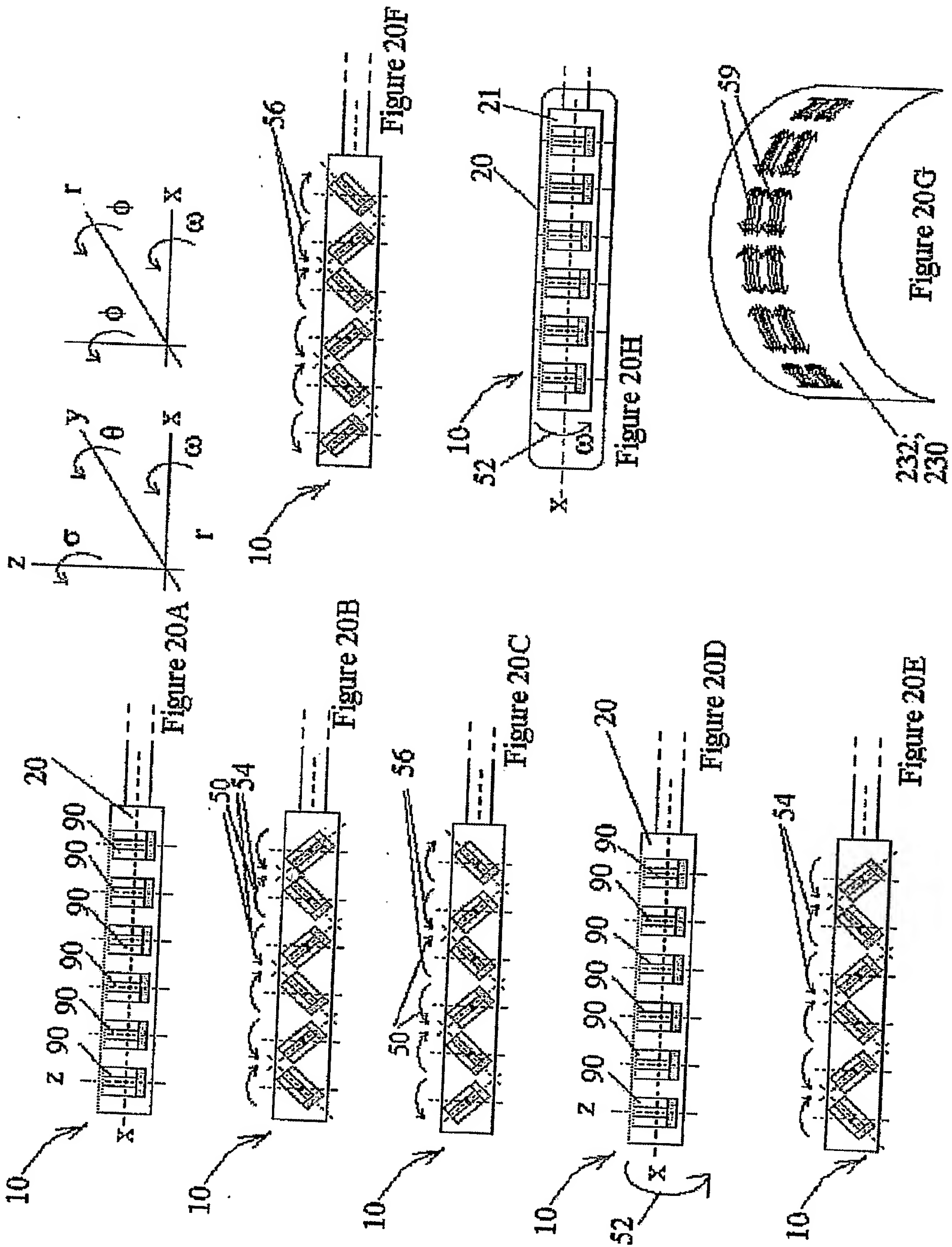


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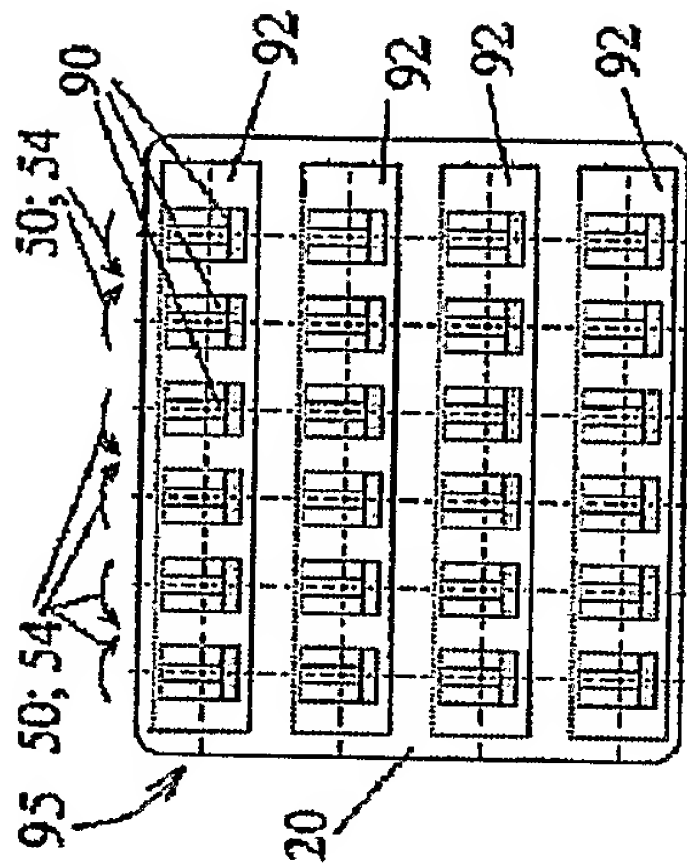


Fig. 22A

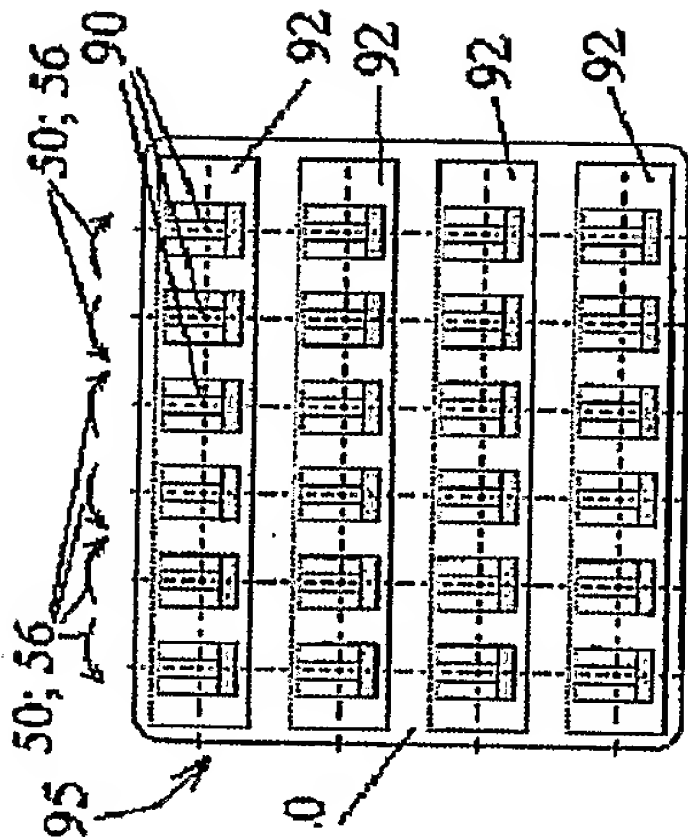


Fig. 22B

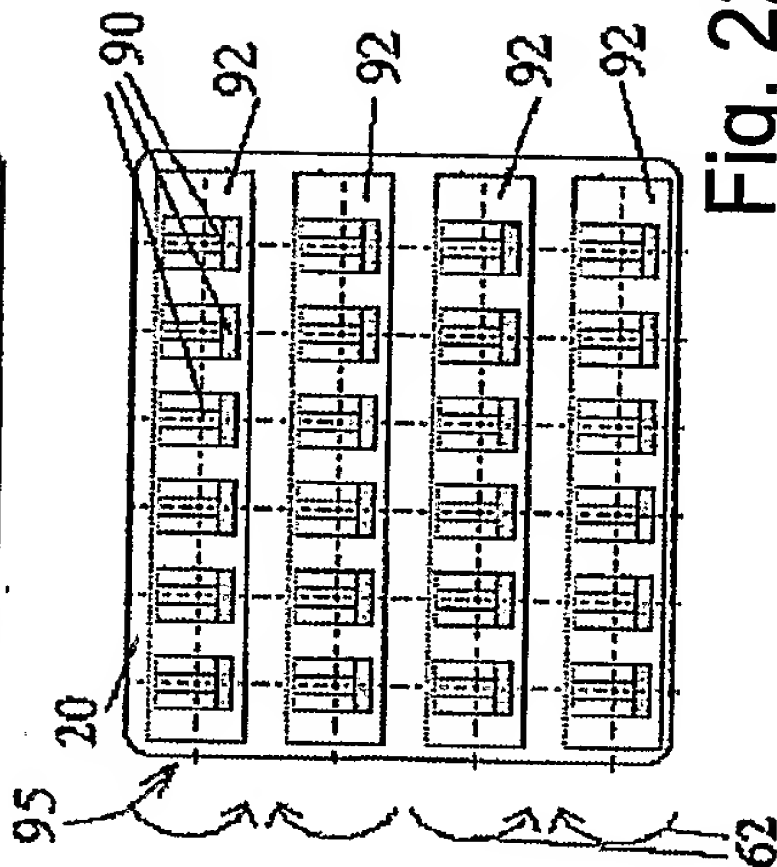


Fig. 22C

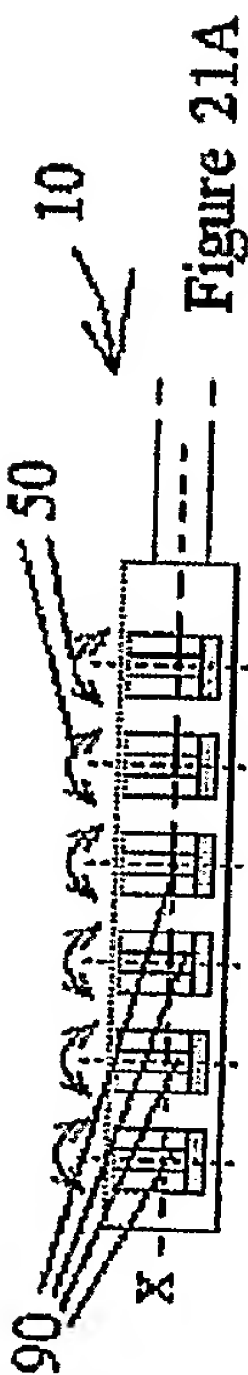


Figure 21A

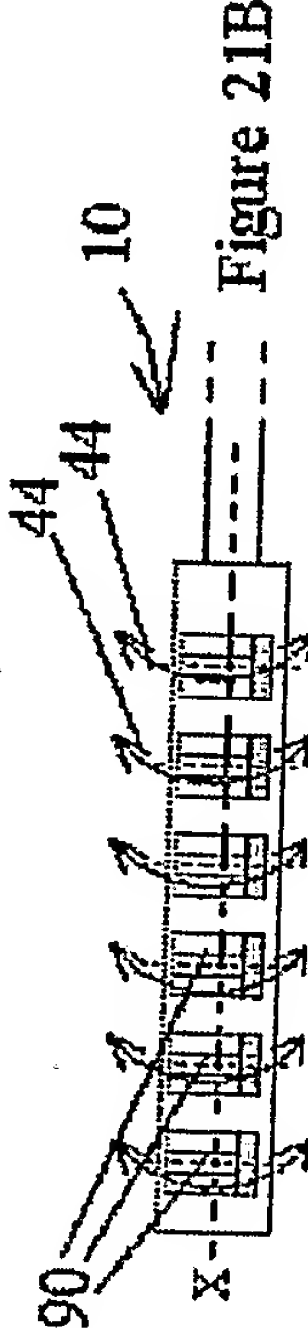


Figure 21B

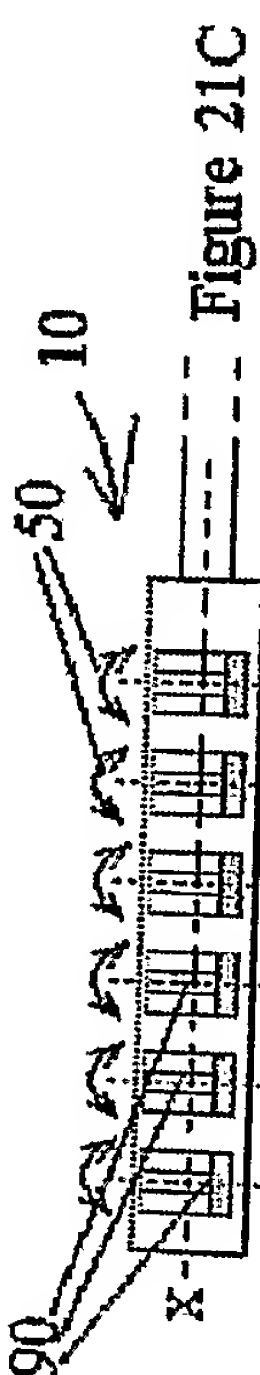


Figure 21C

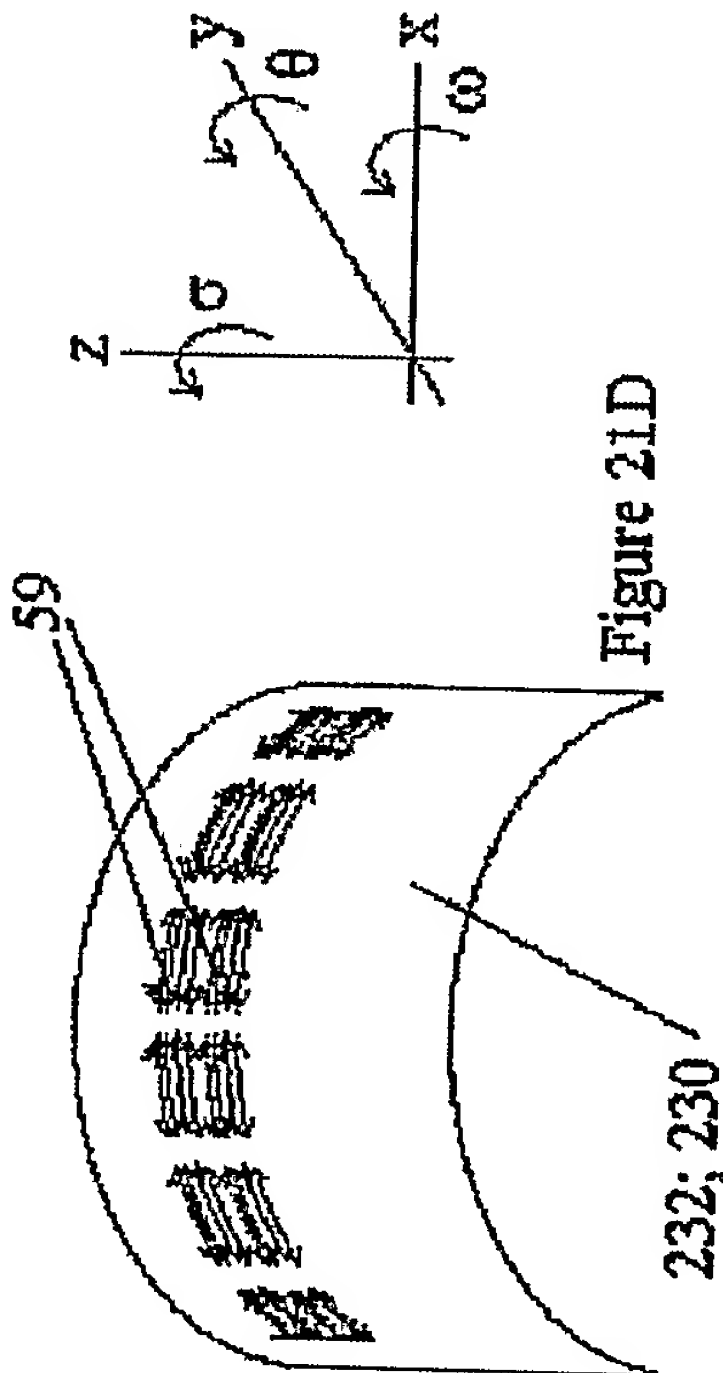


Figure 21D

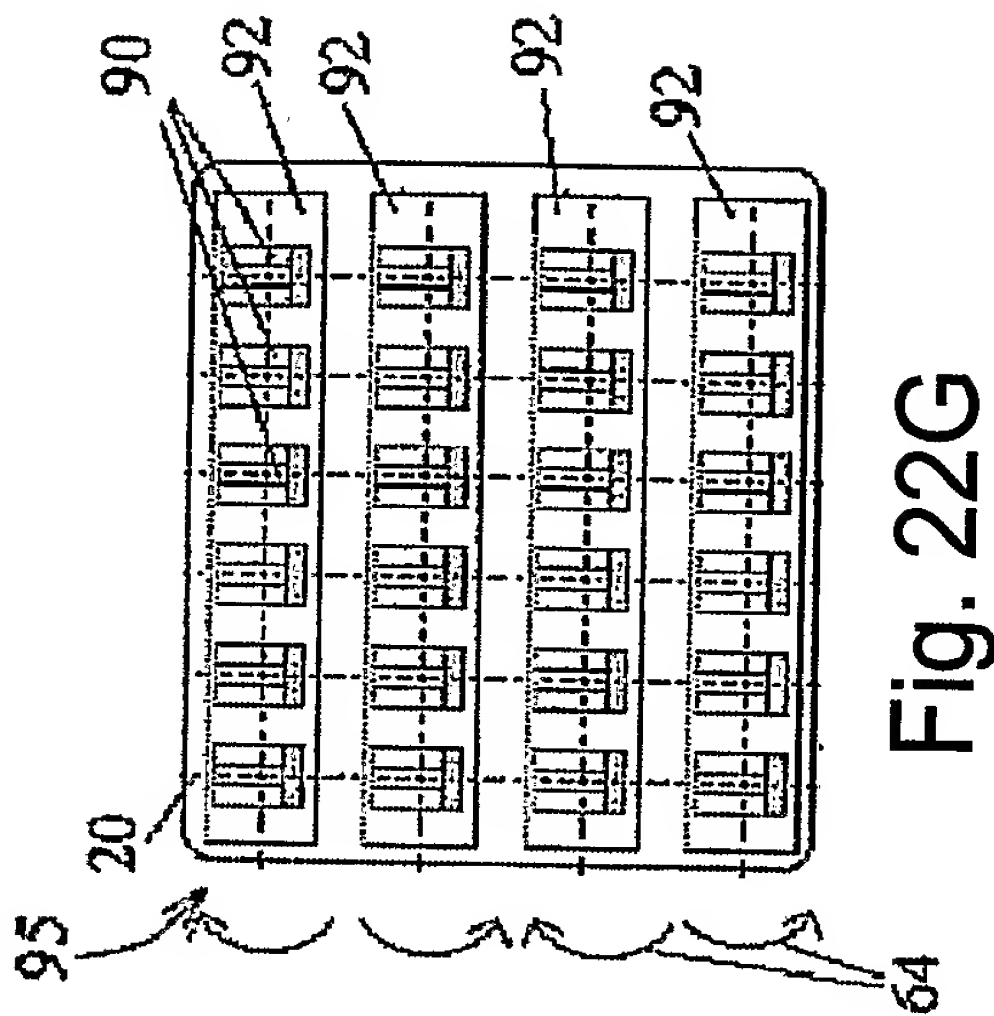


Fig. 22G

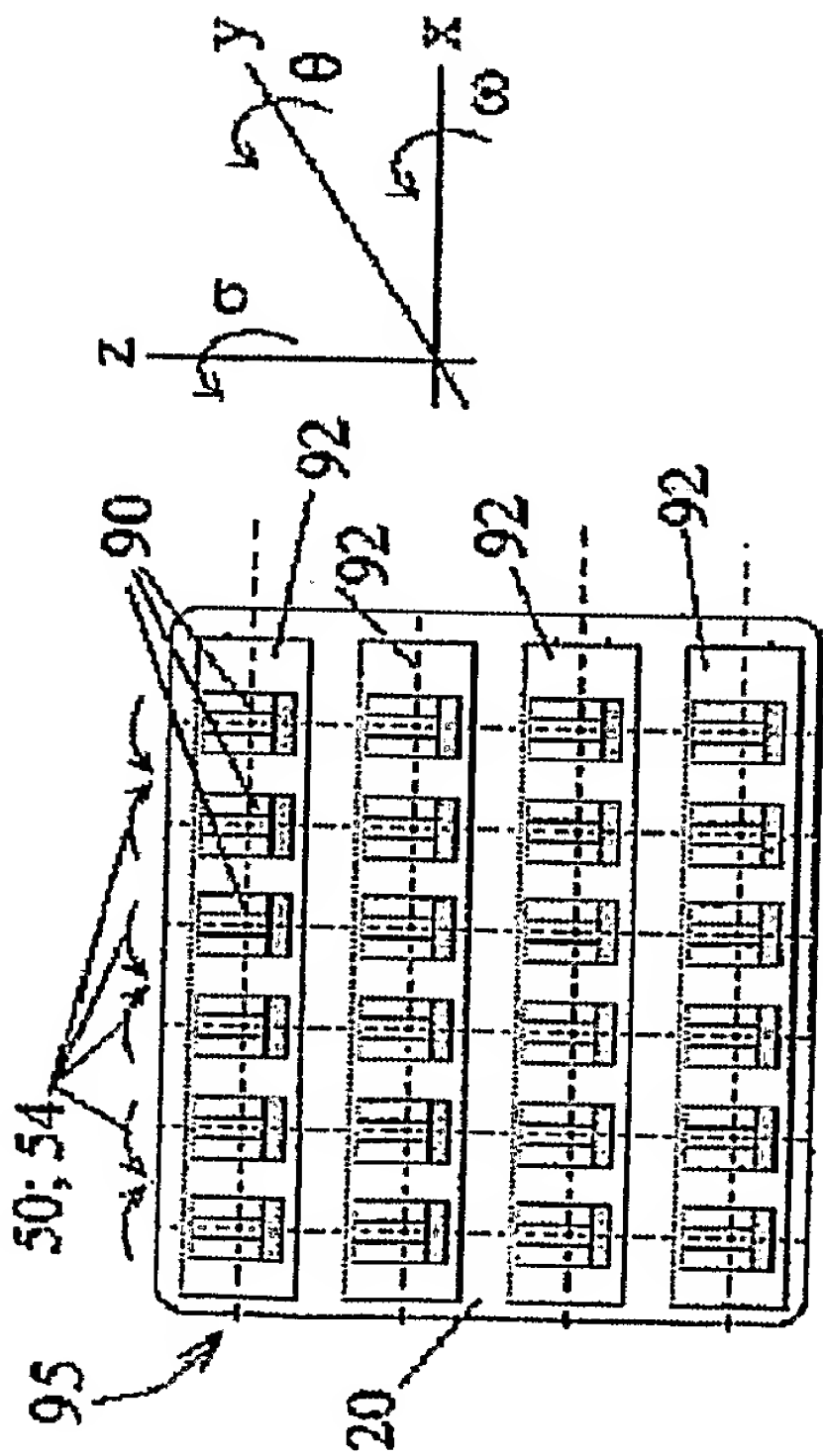
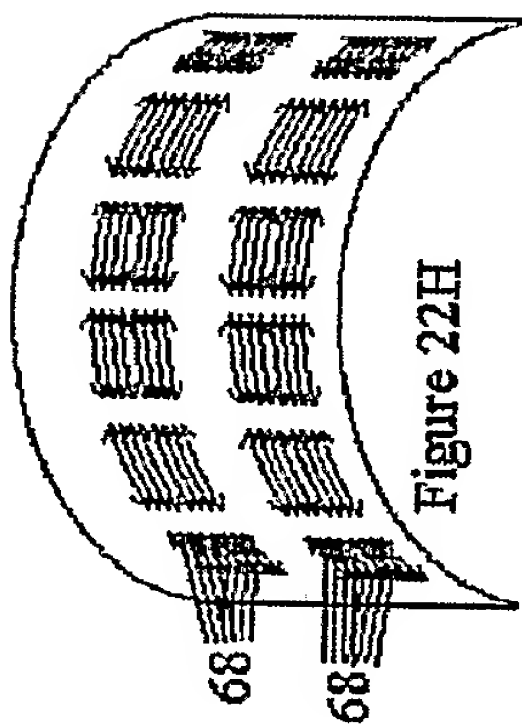
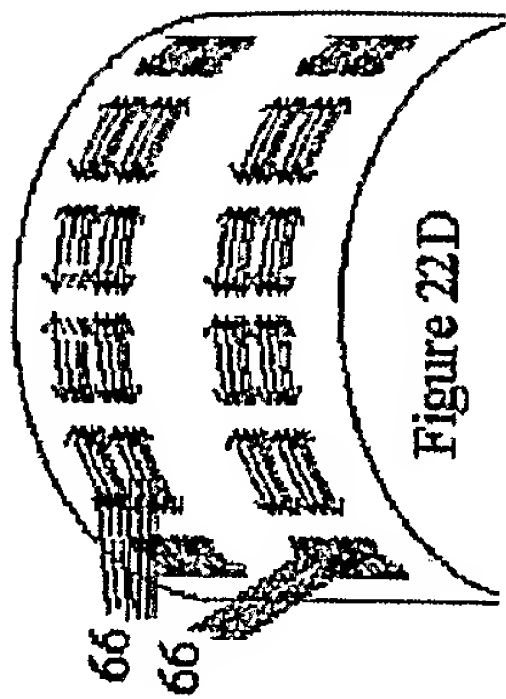


Fig. 22E

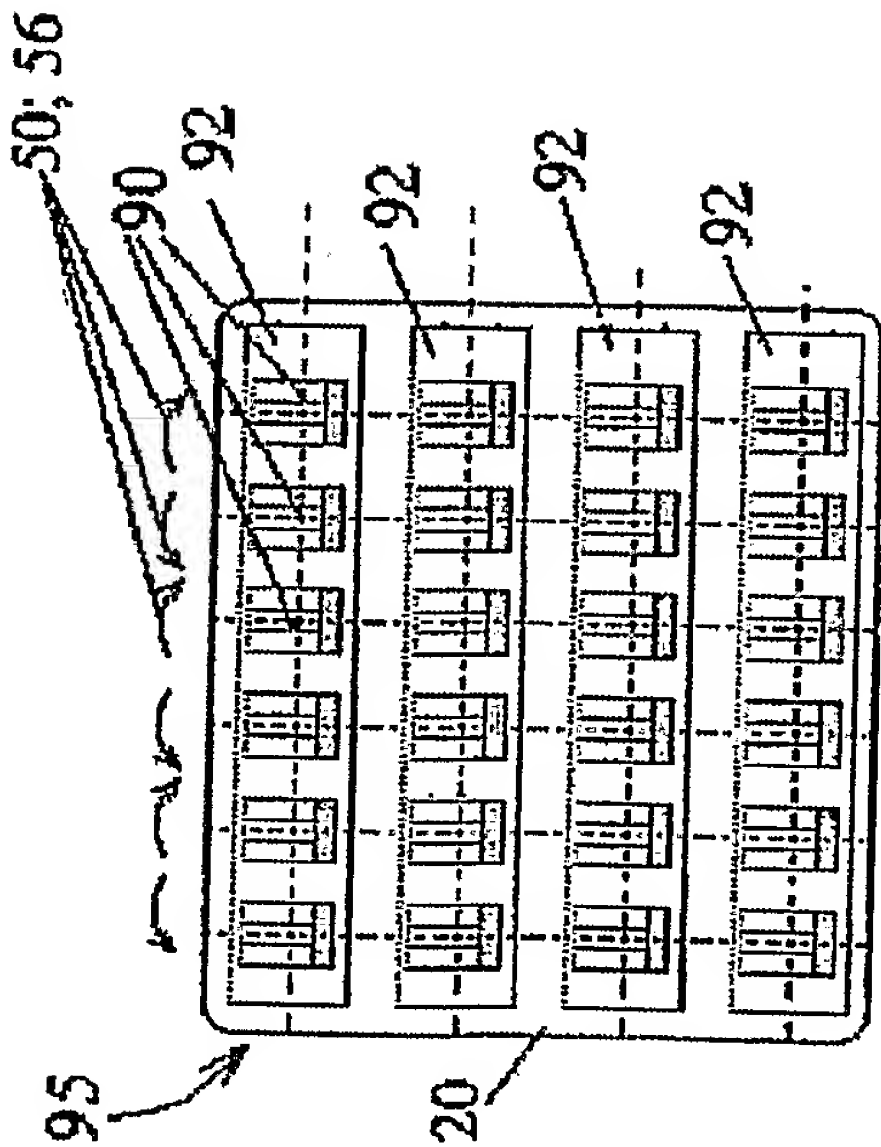


Fig. 22F

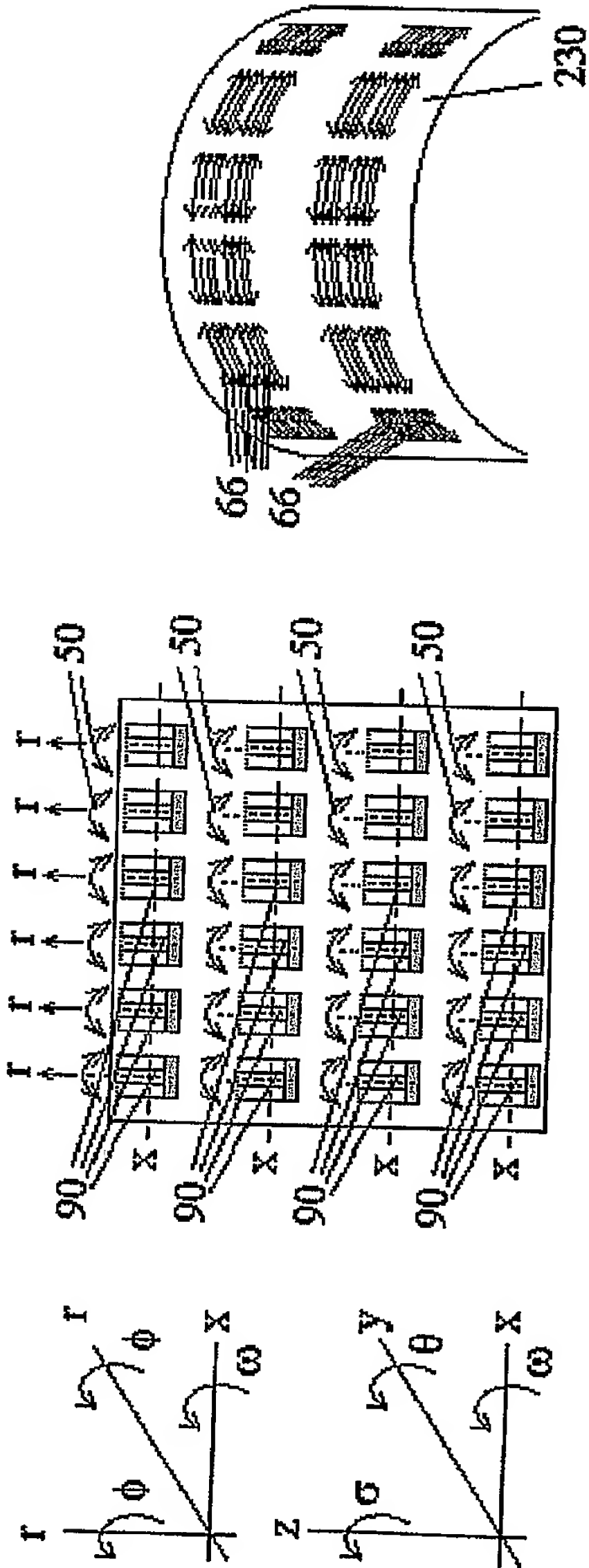


Figure 22J

Figure 22I

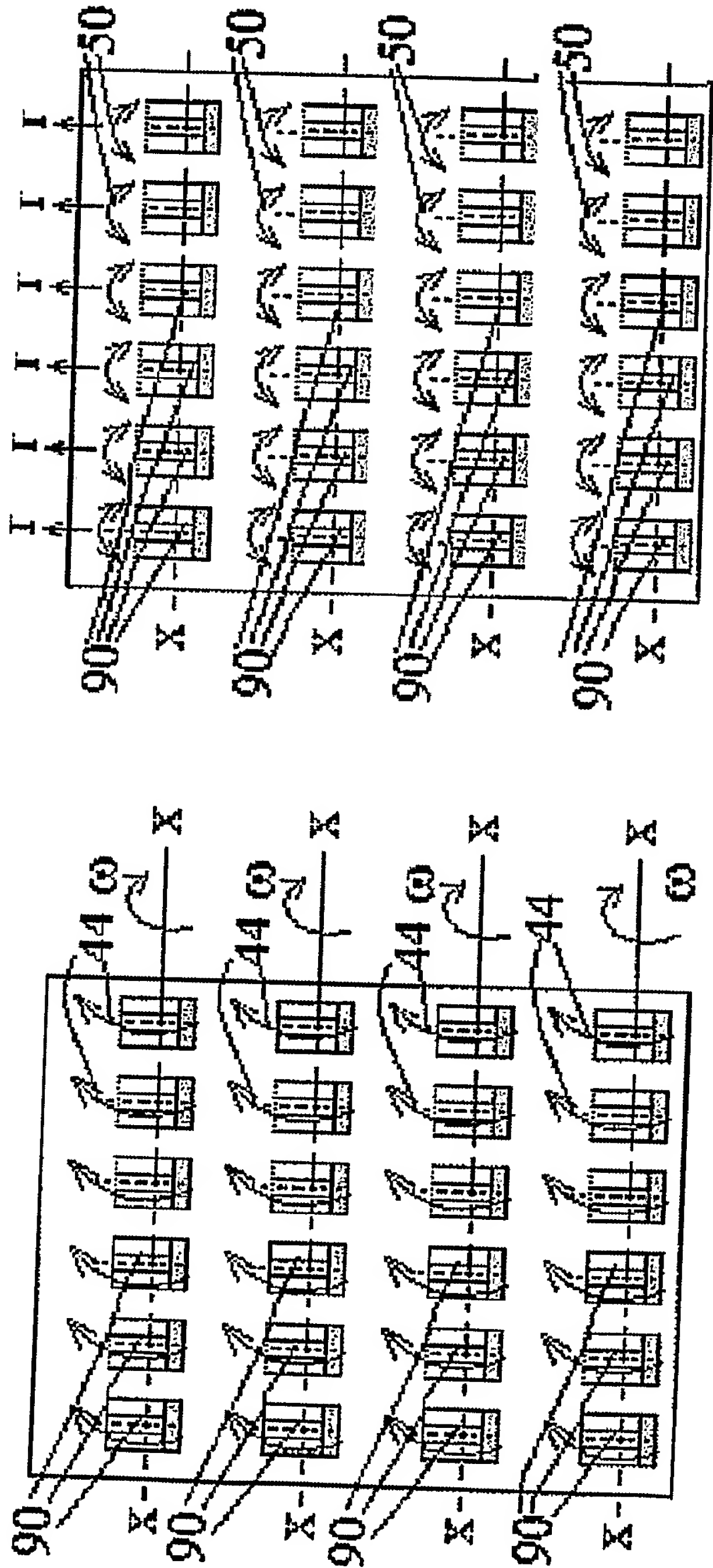


Fig. 22K

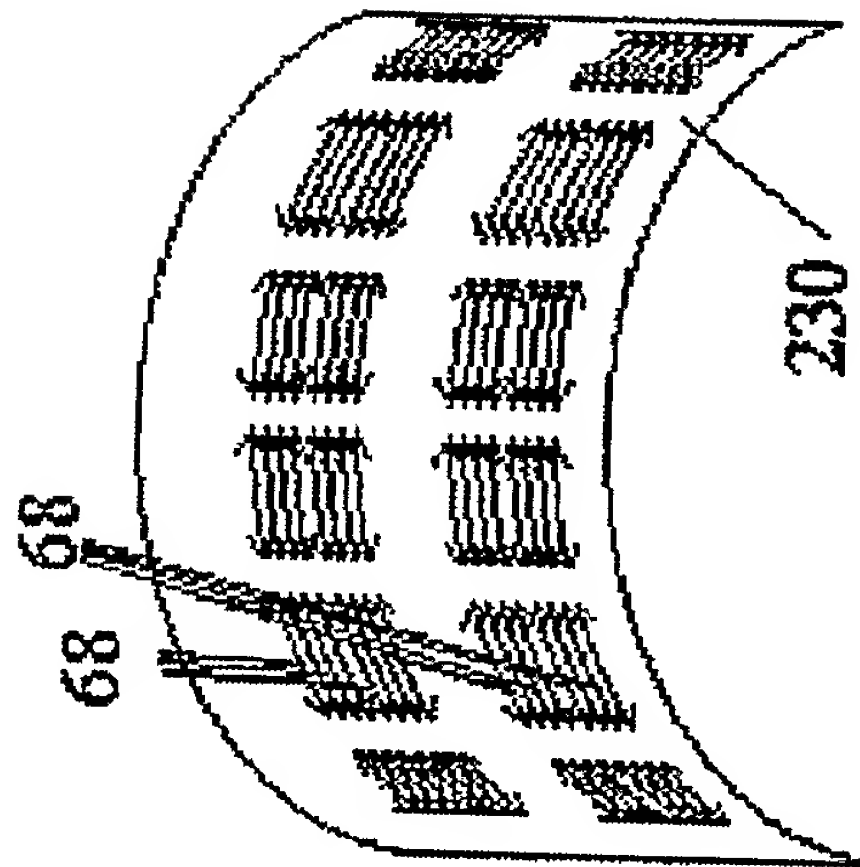
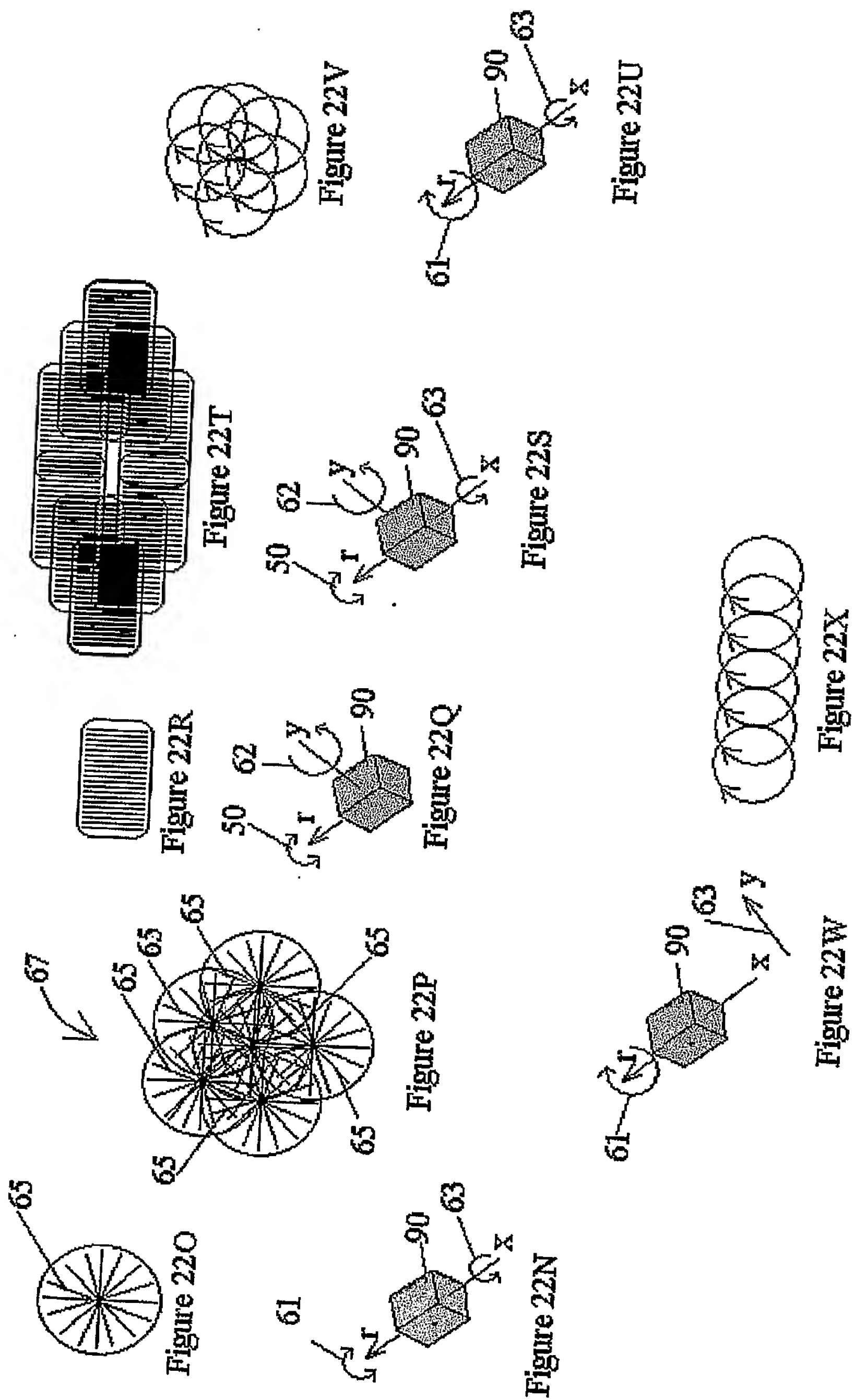


Fig. 22M

Fig. 22L



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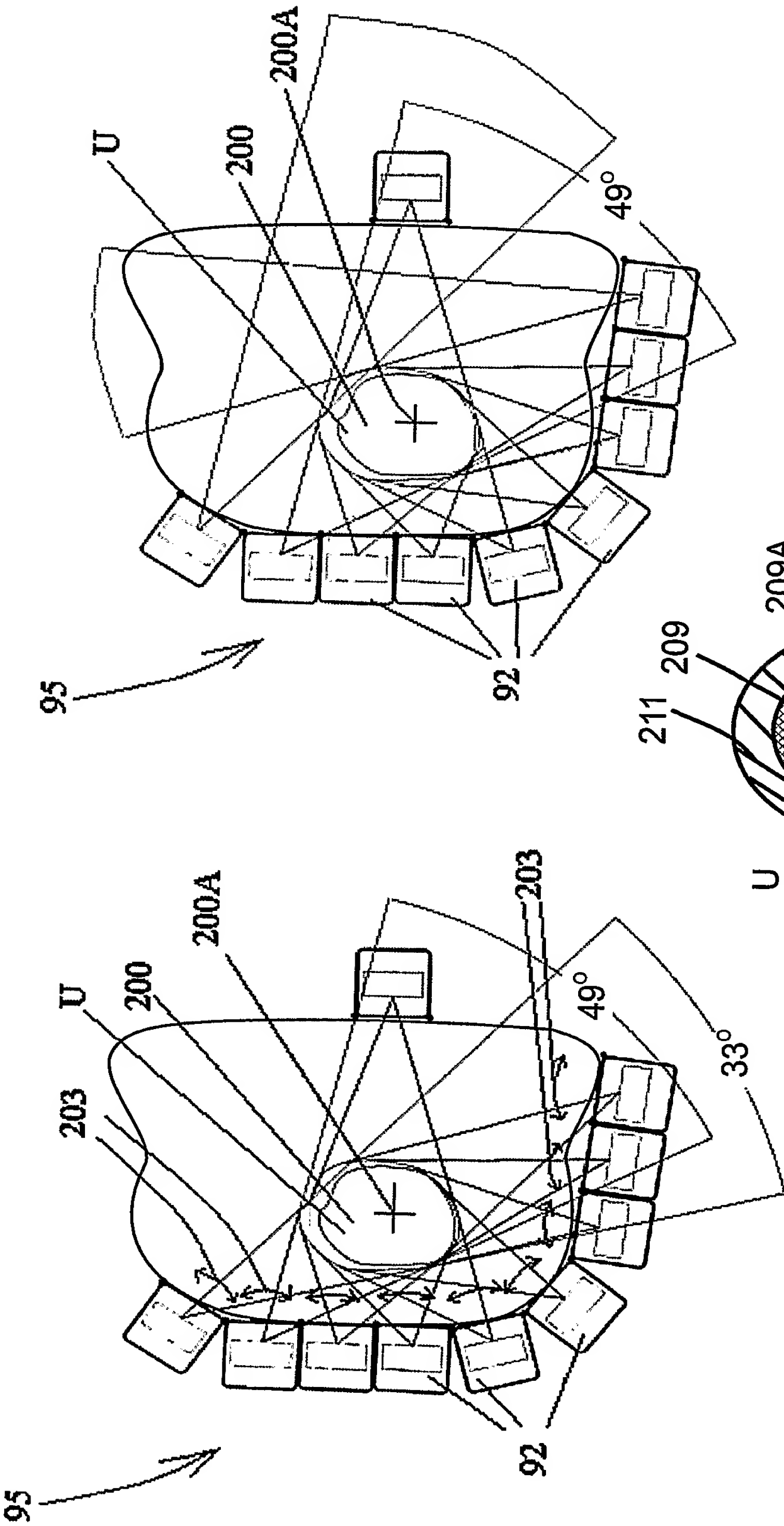


Fig. 22Z

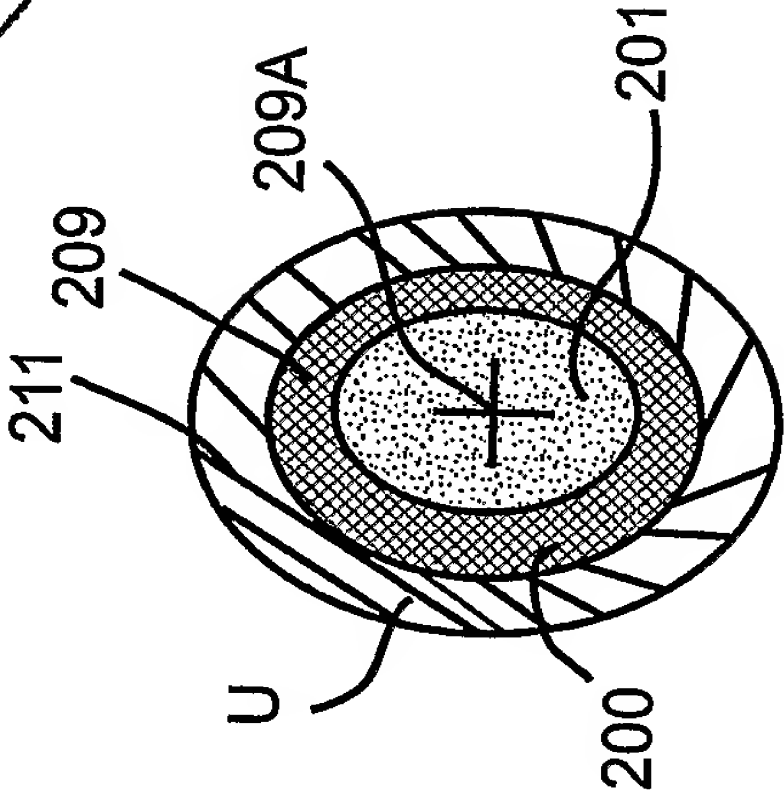
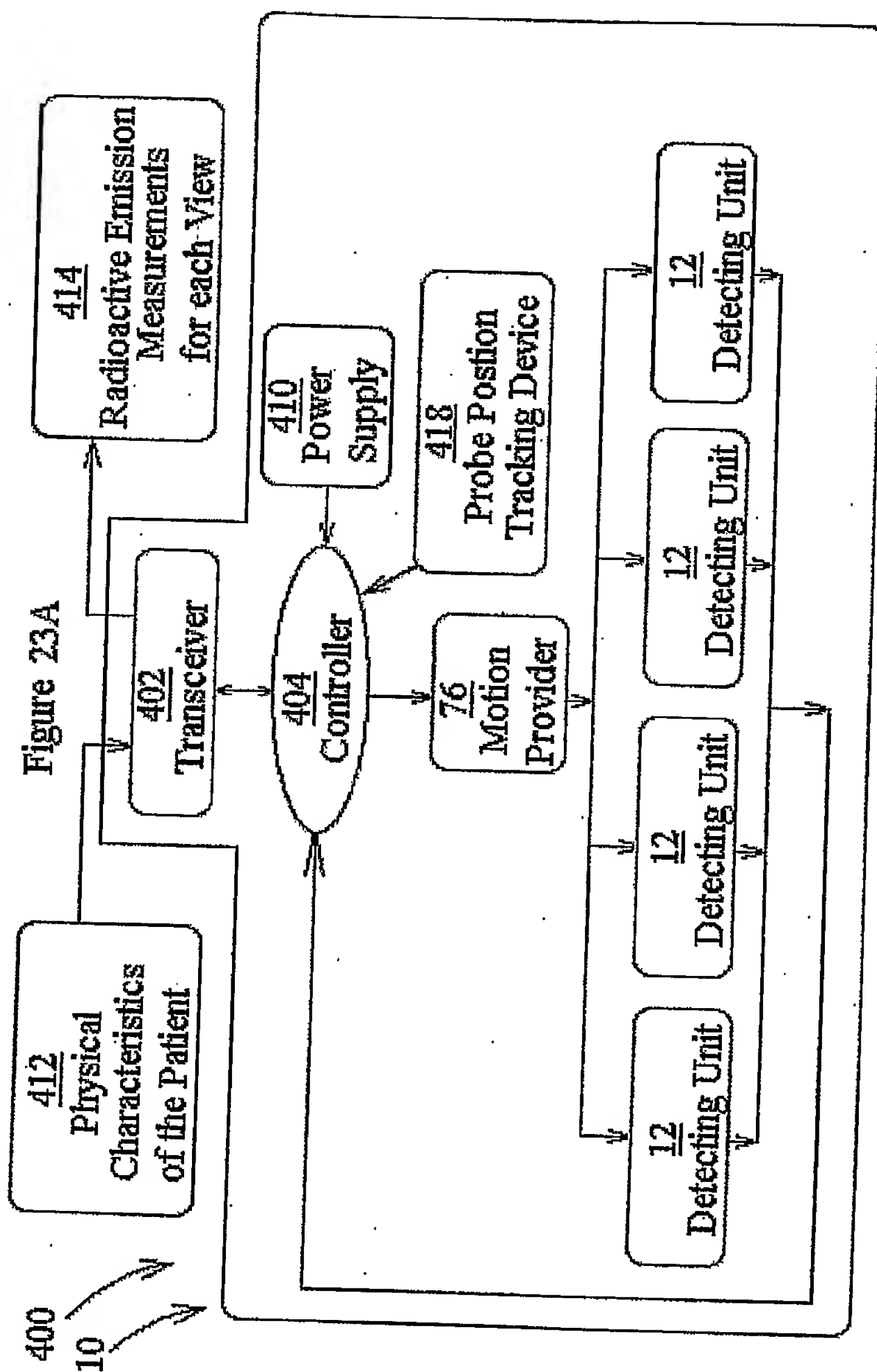
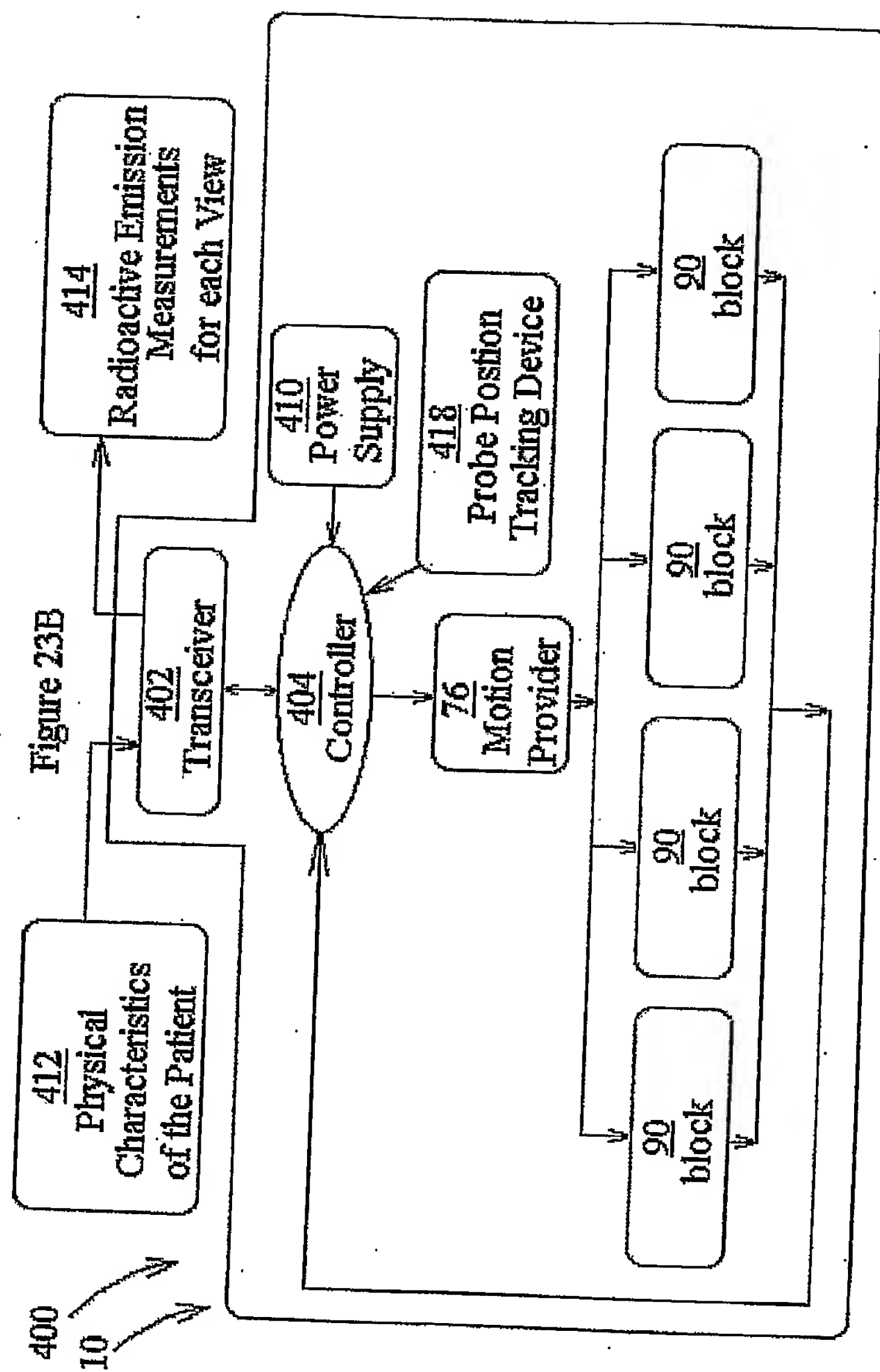


Fig. 22AA

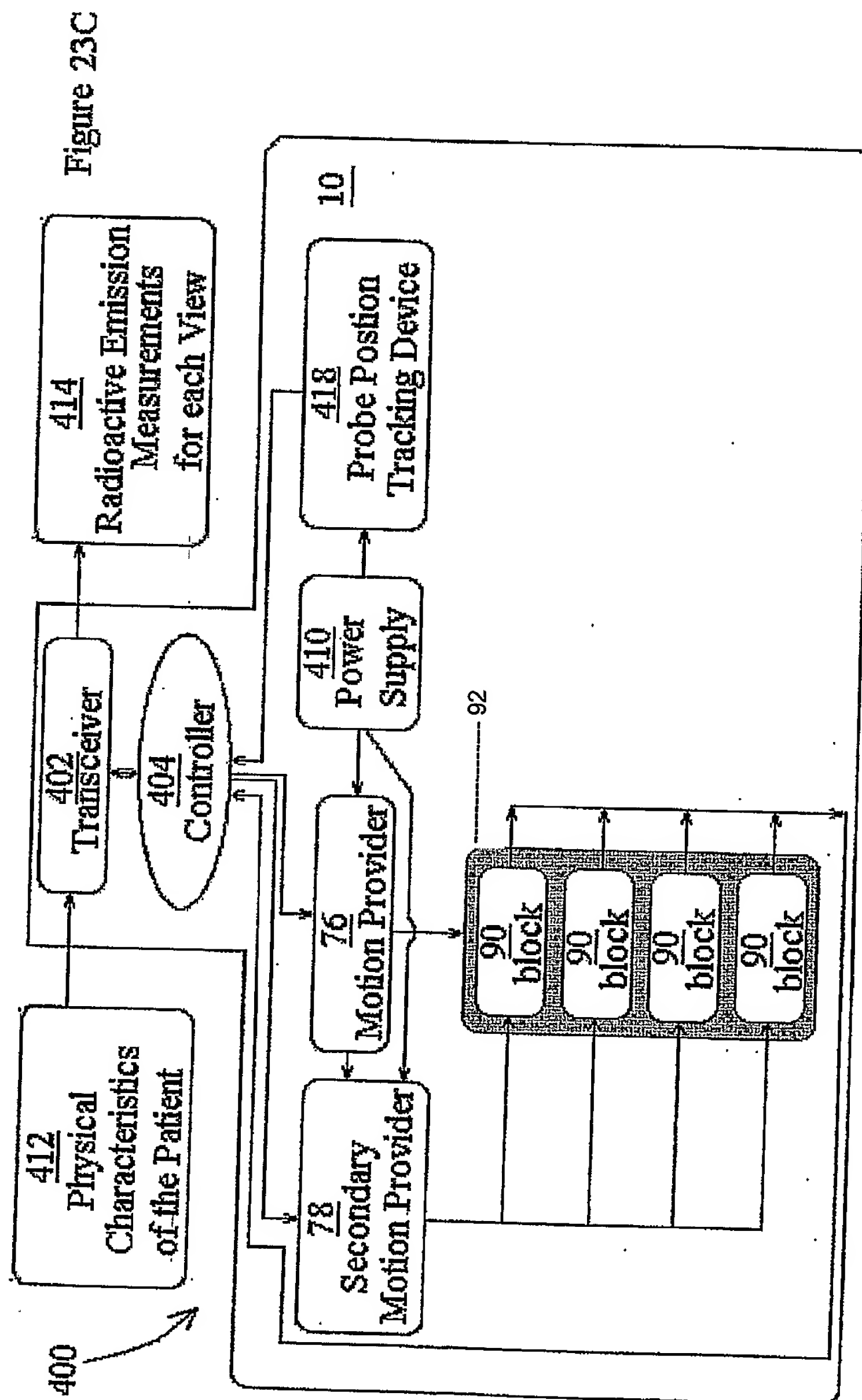
Fig. 22Y



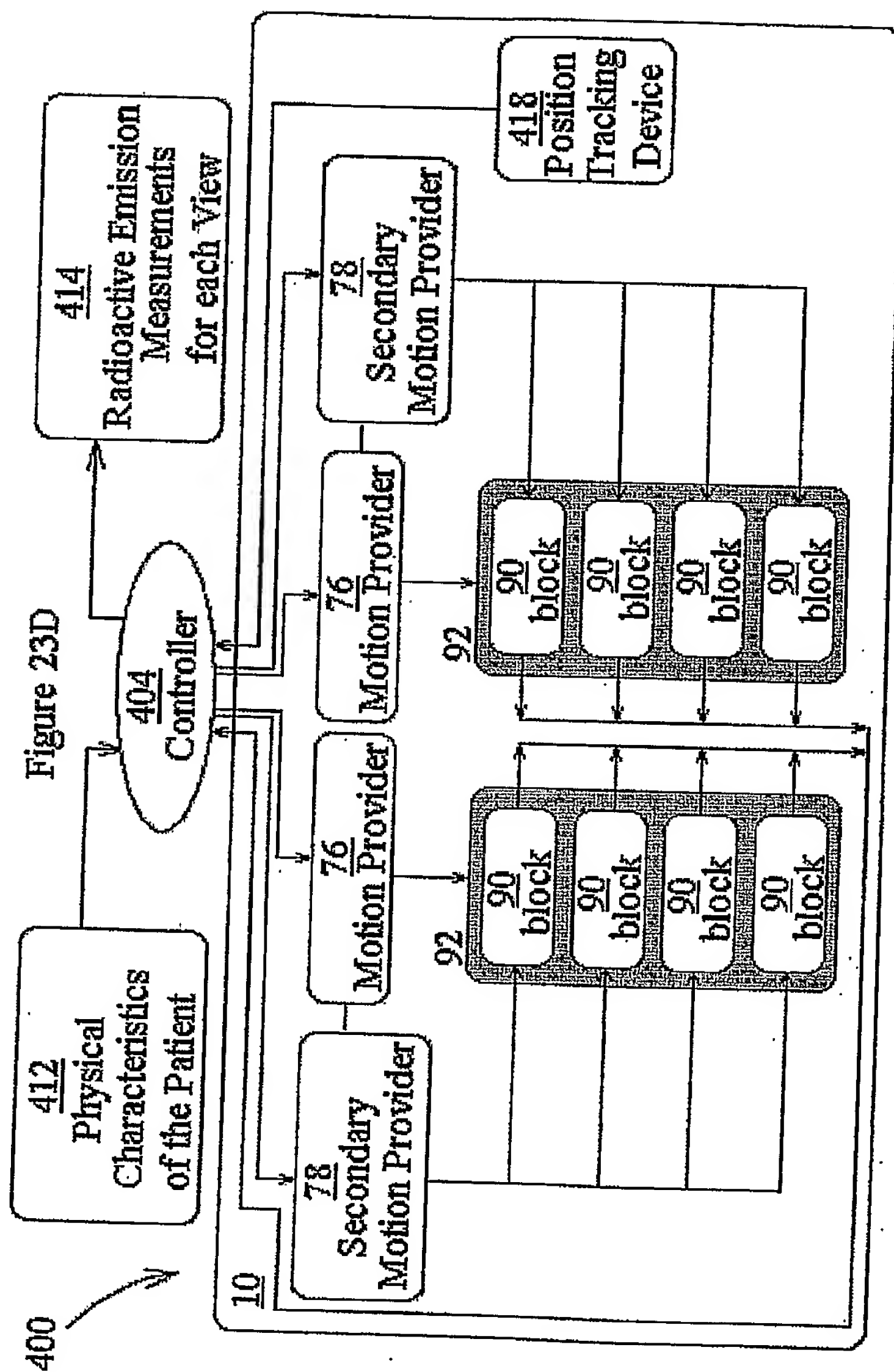




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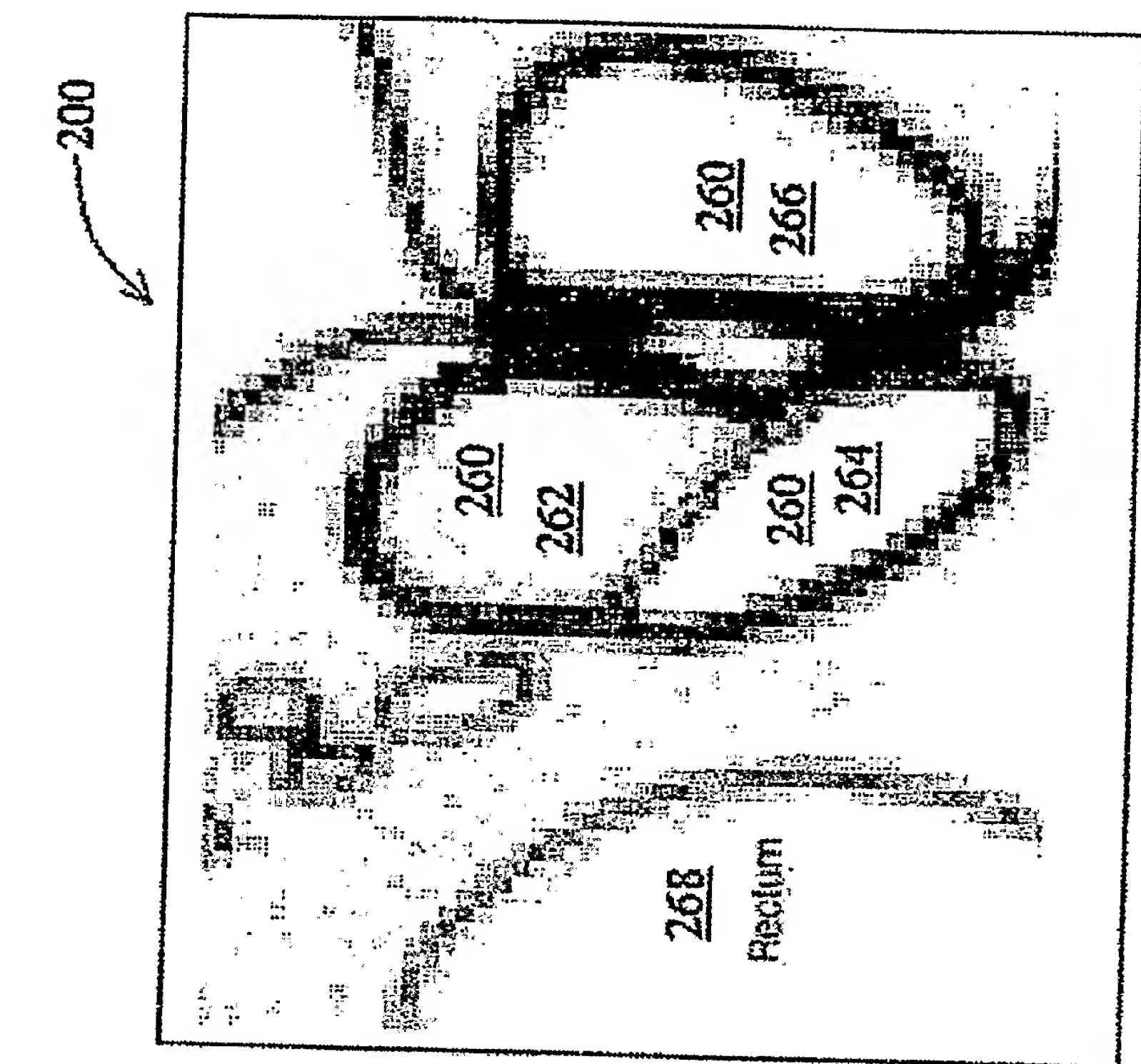


Fig. 24A

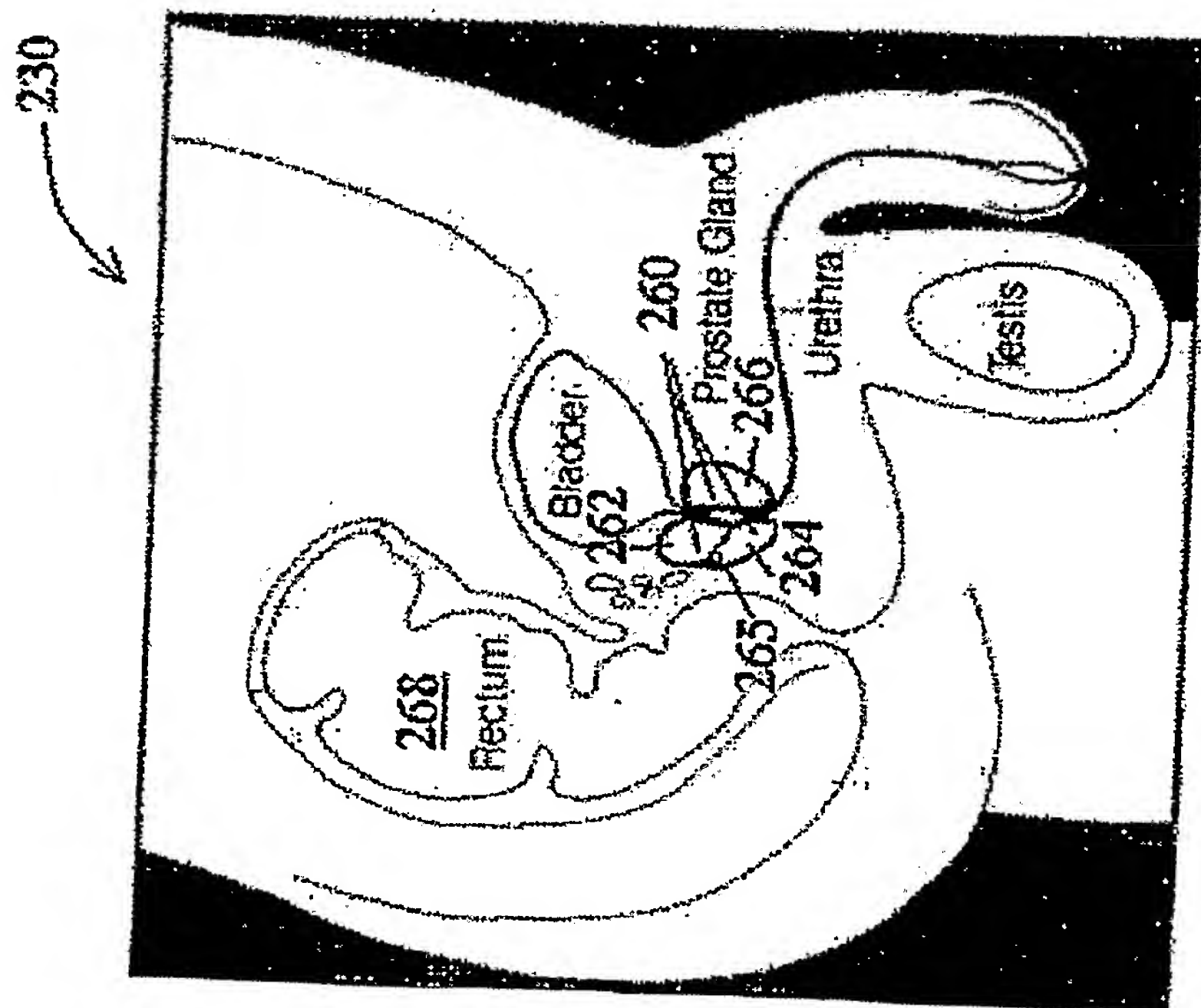


Fig. 24B

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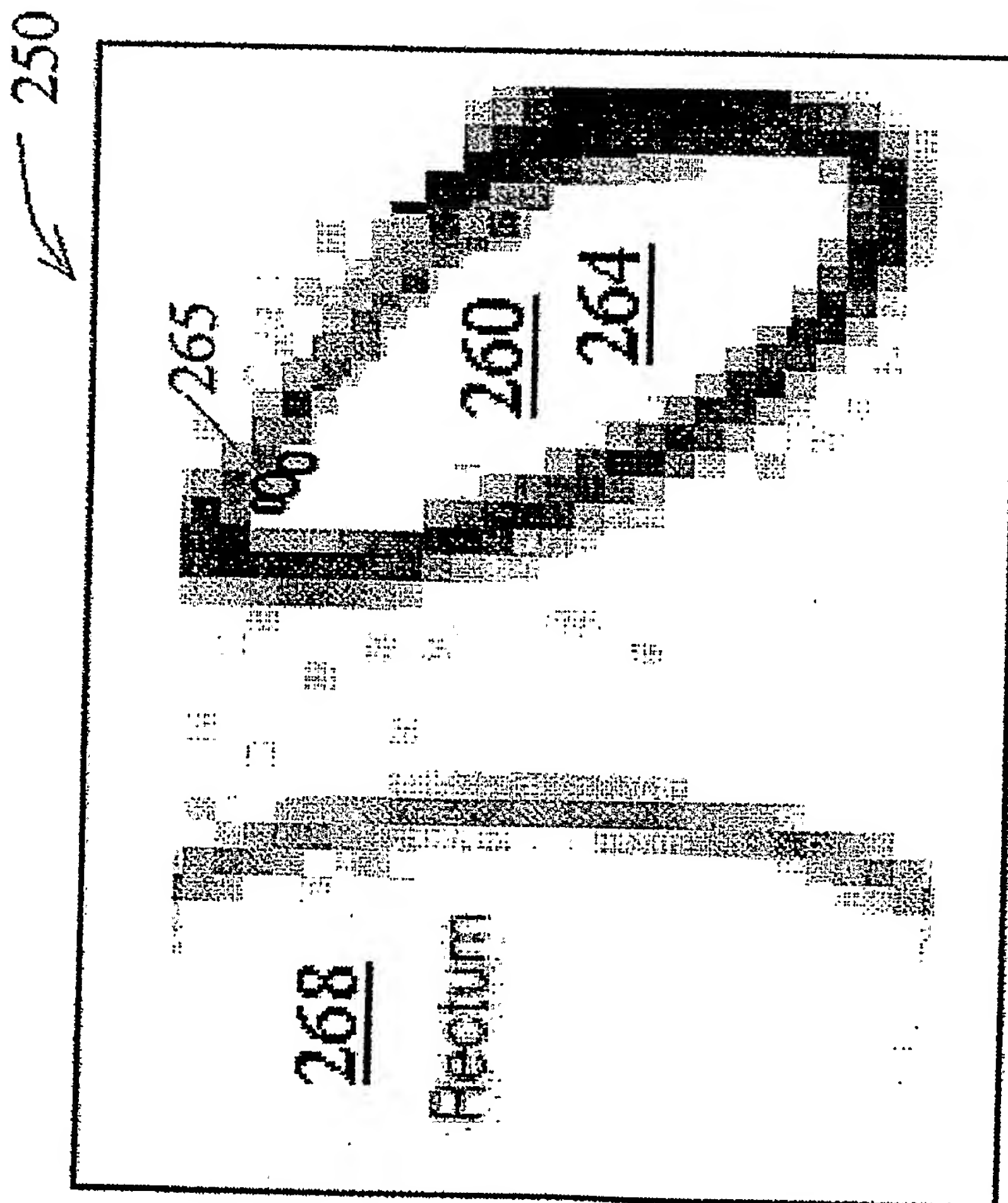
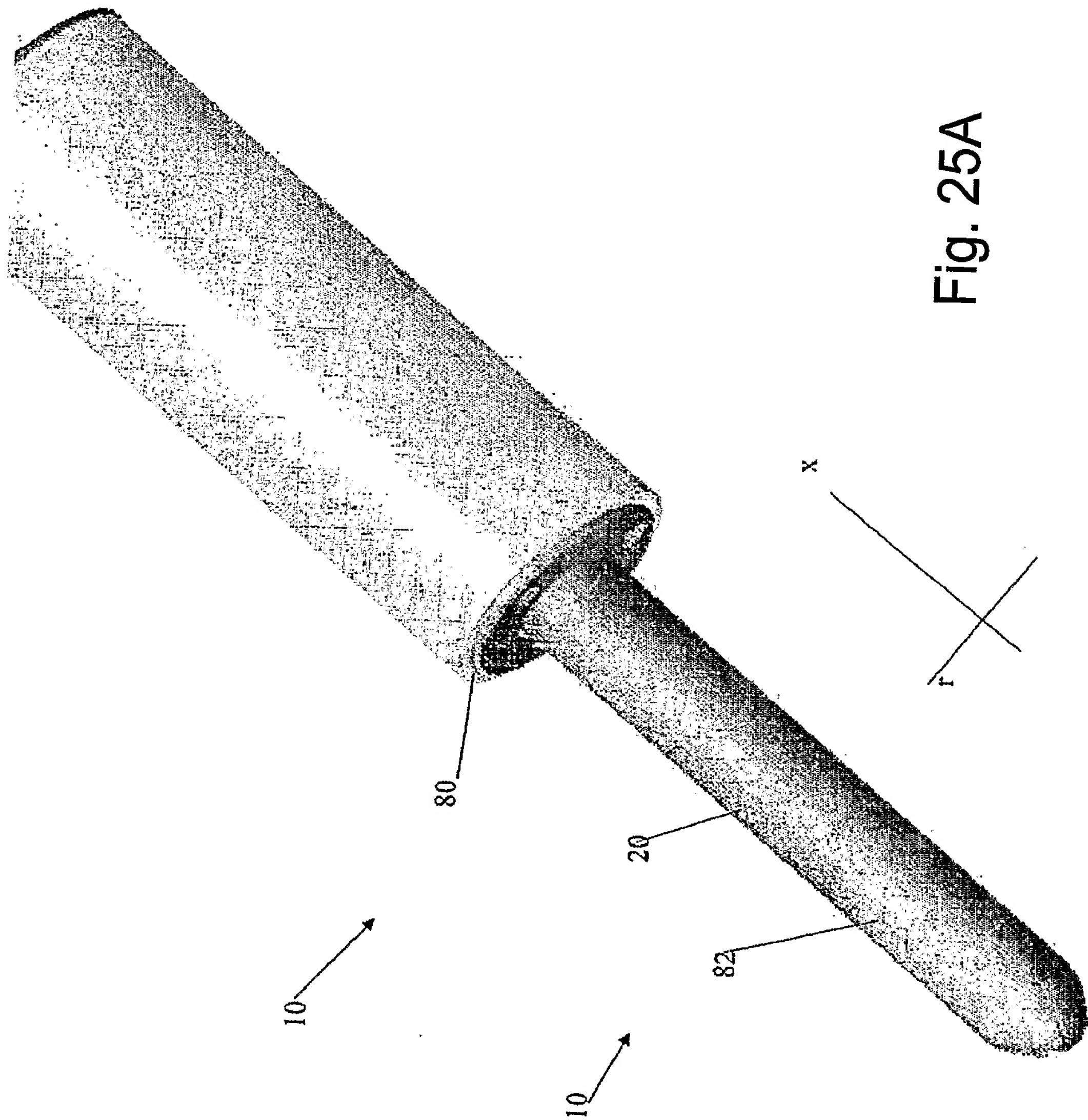


Fig. 24C





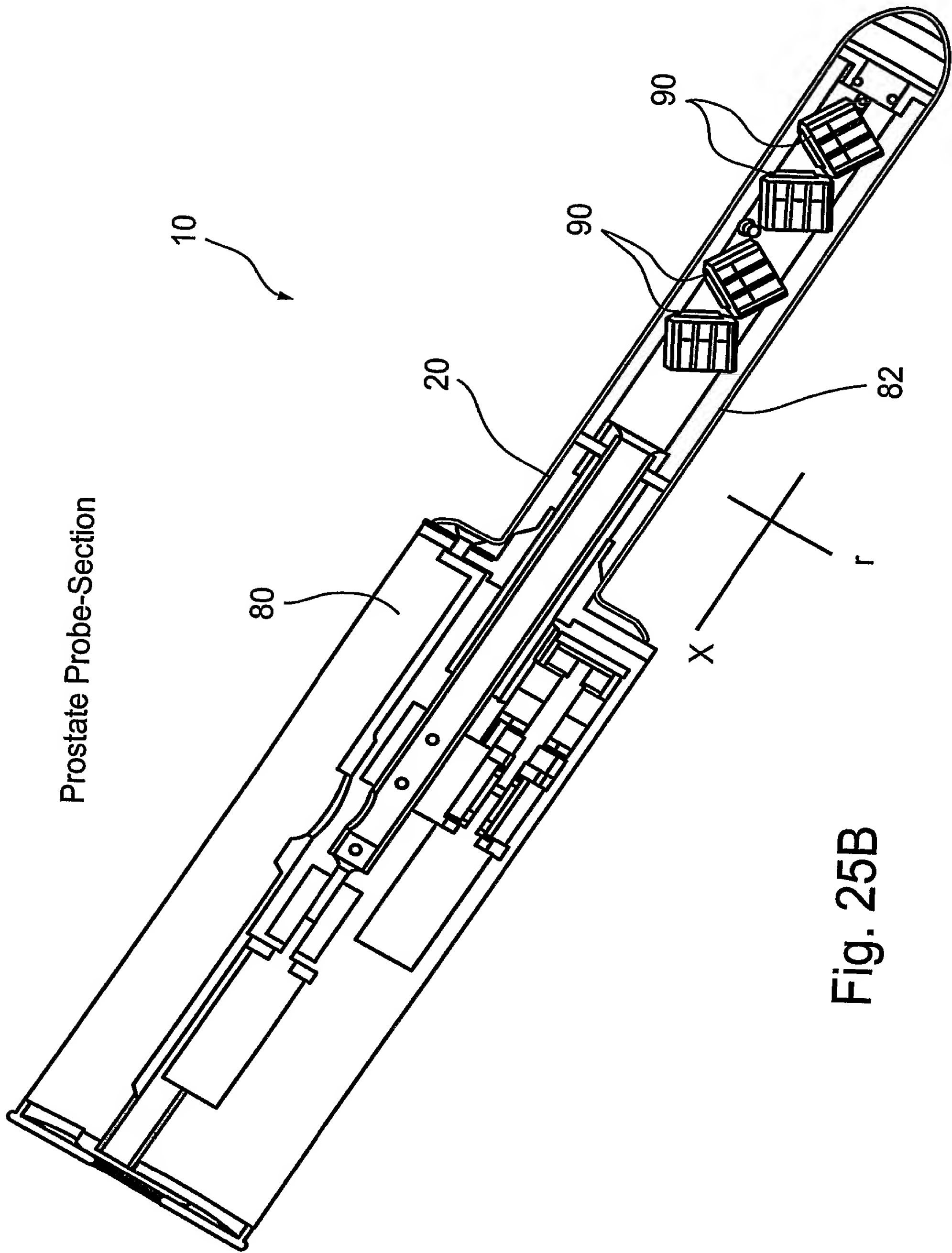


Fig. 25B

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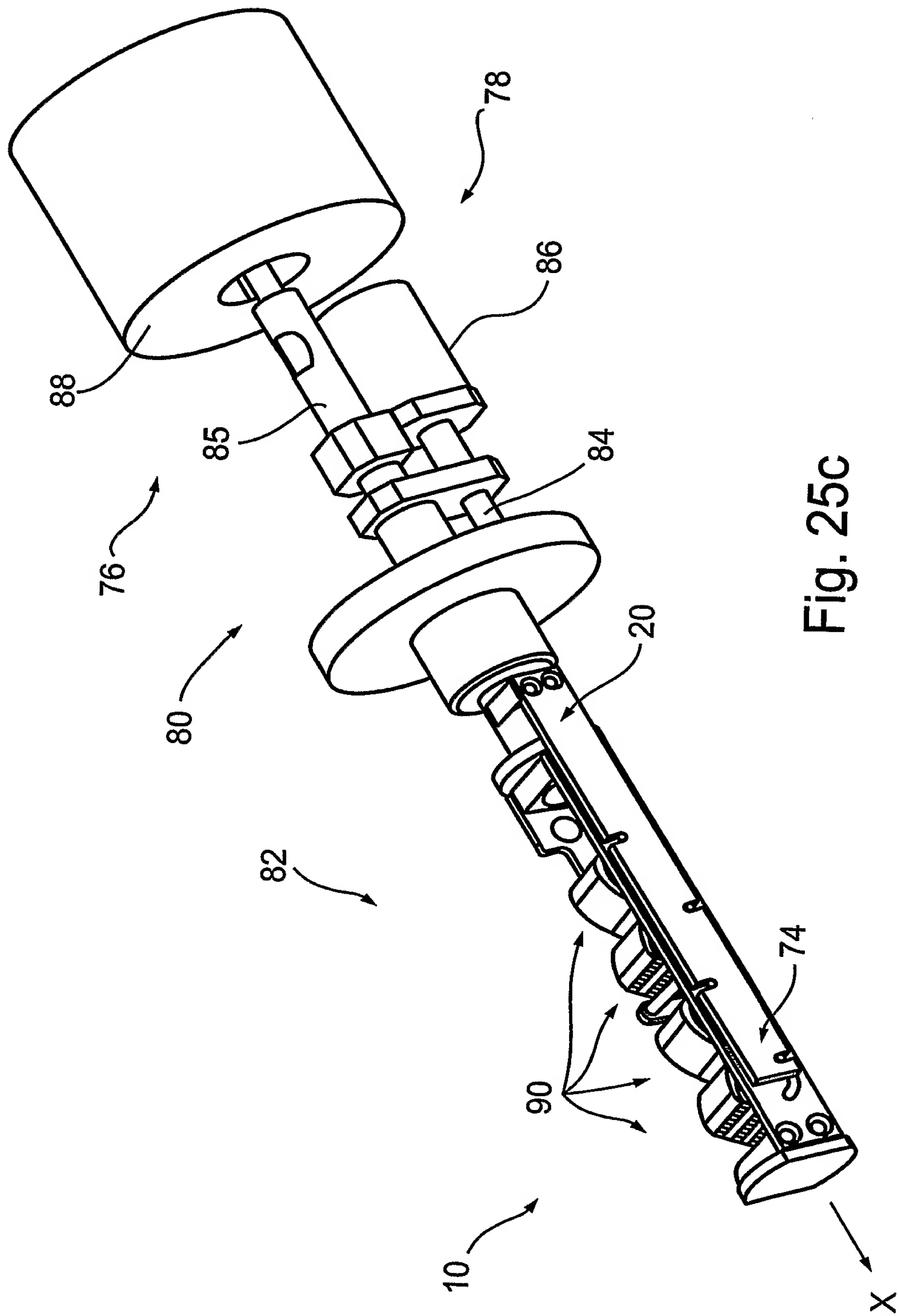


Fig. 25c

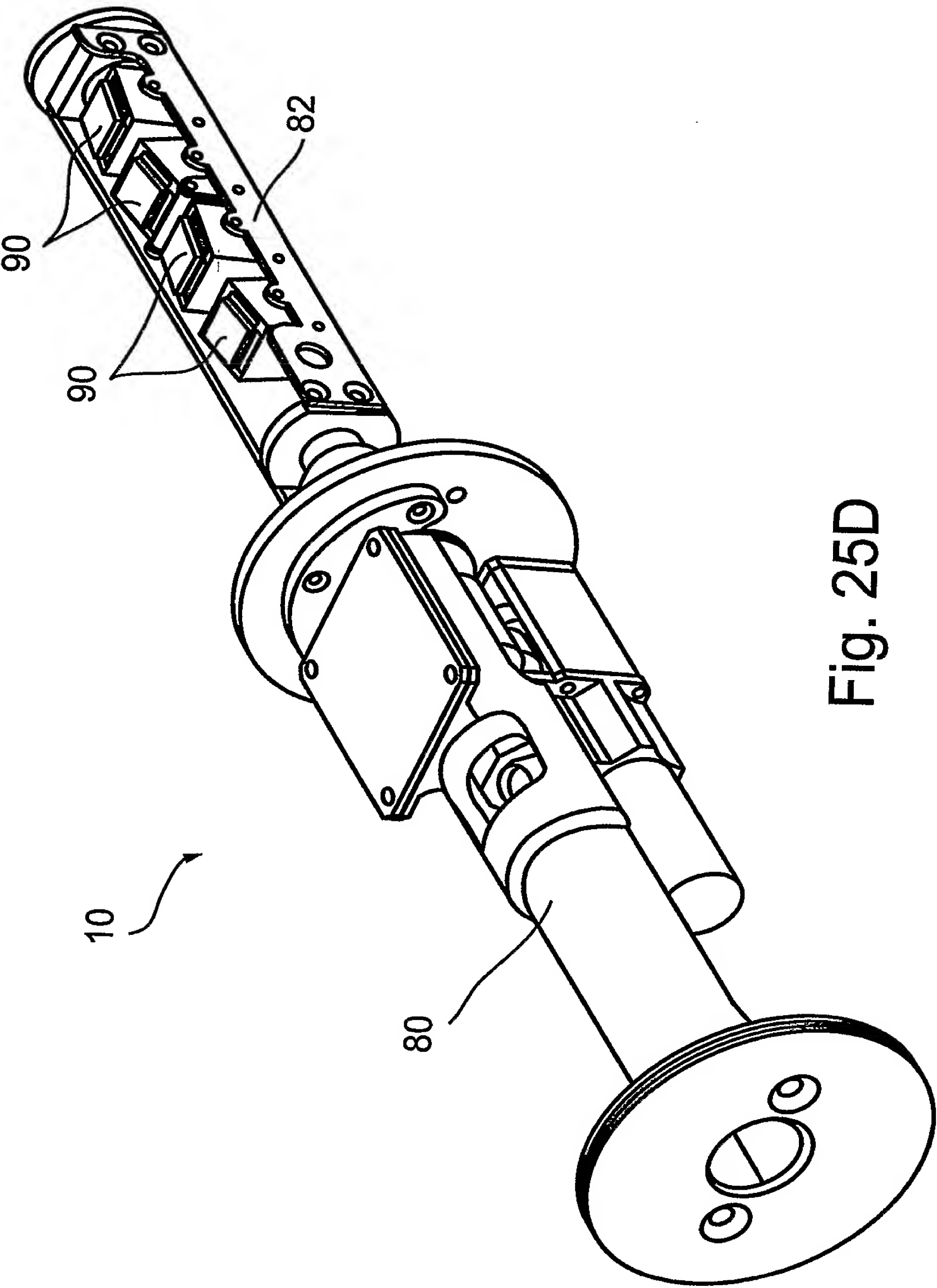


Fig. 25D

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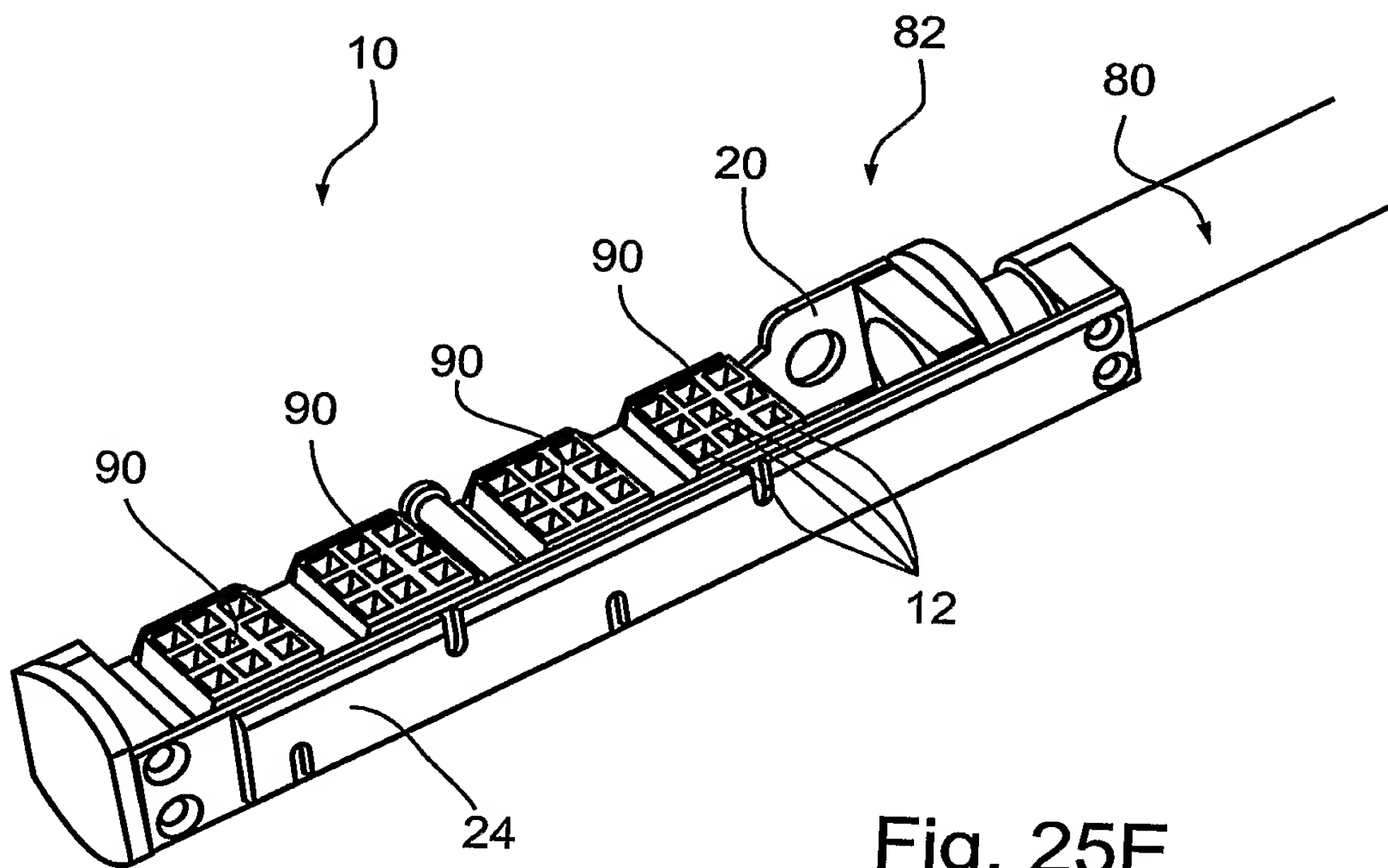


Fig. 25E

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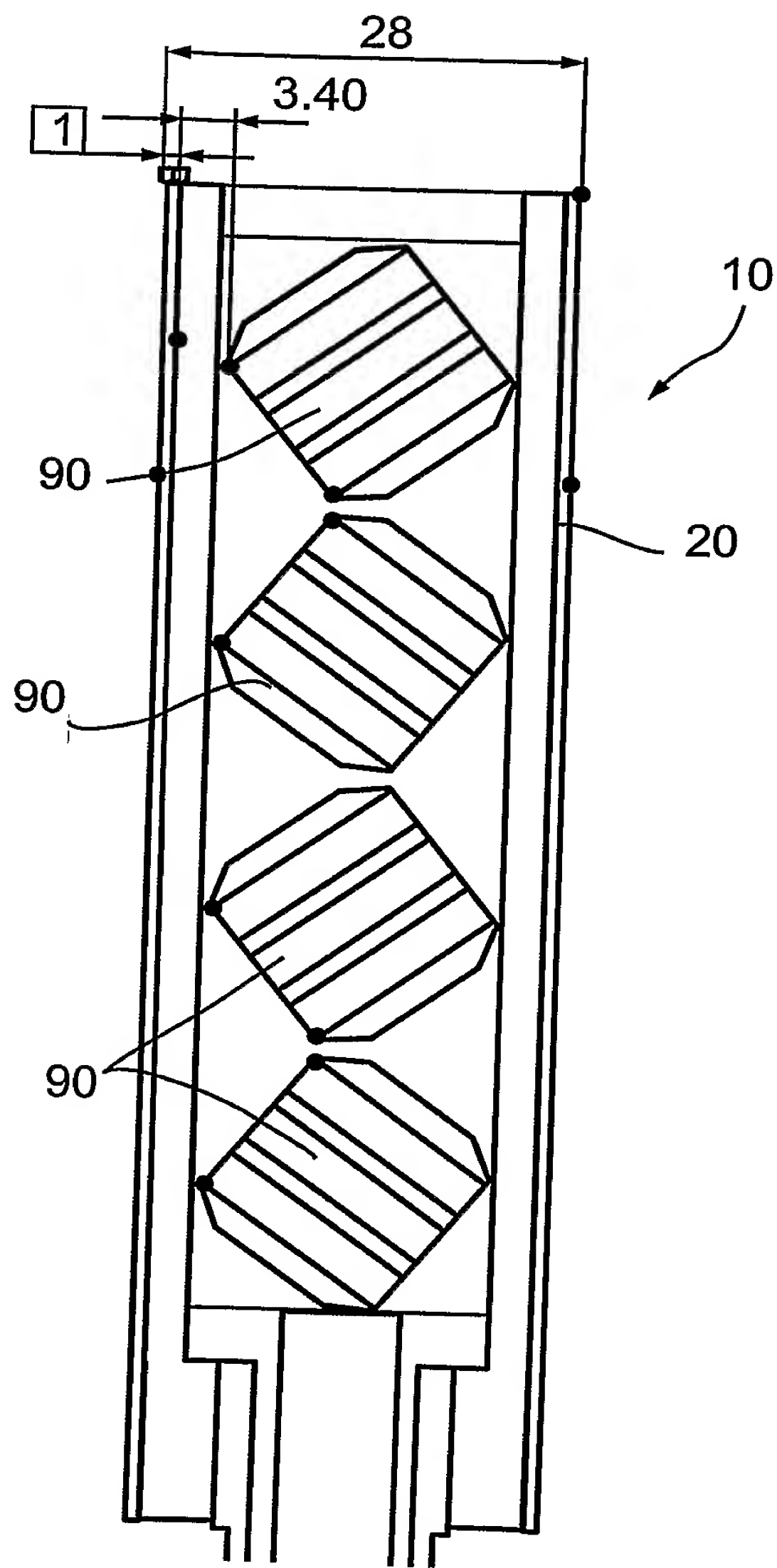


Fig. 26

Ultrasound-Nuclear trans-rectal probe

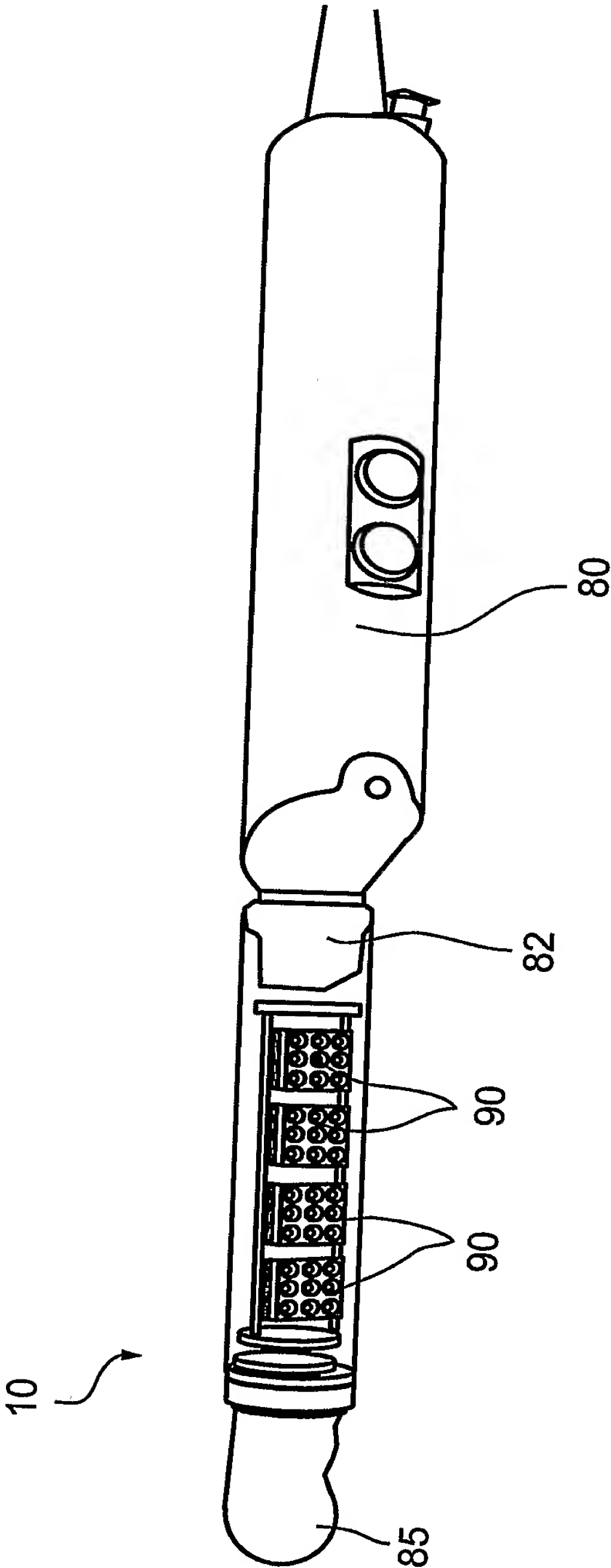


Fig. 27

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## Operation of US-Nuclear transrectal probe

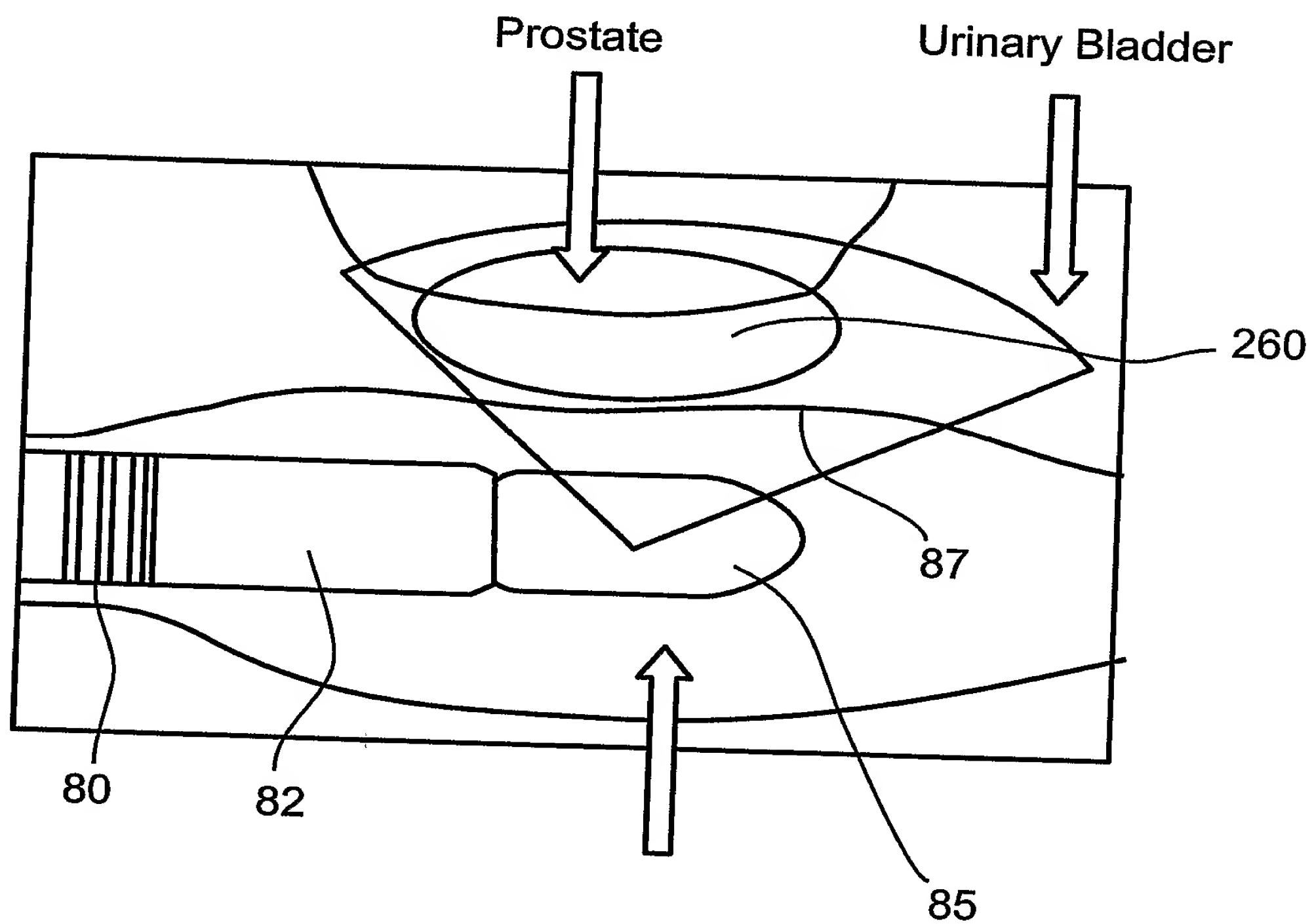


Fig. 28



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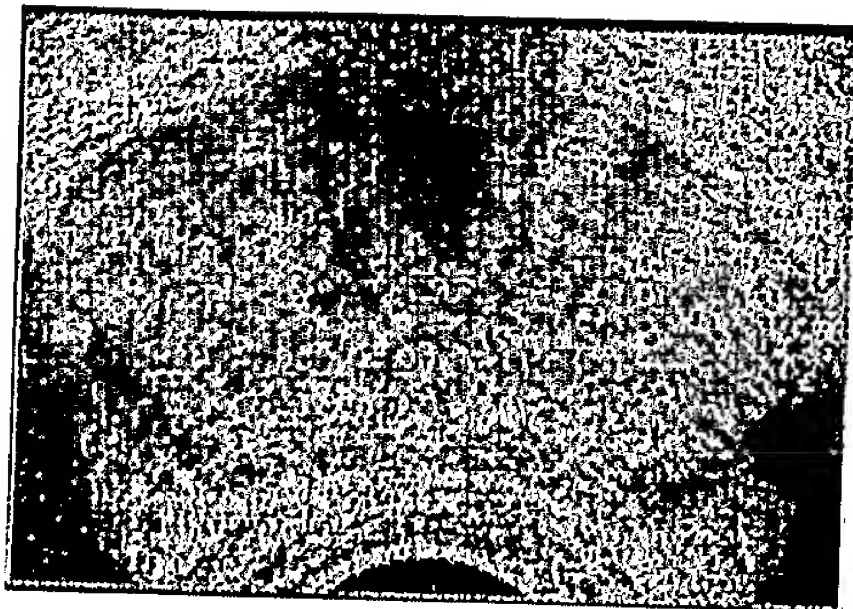


Fig. 29A

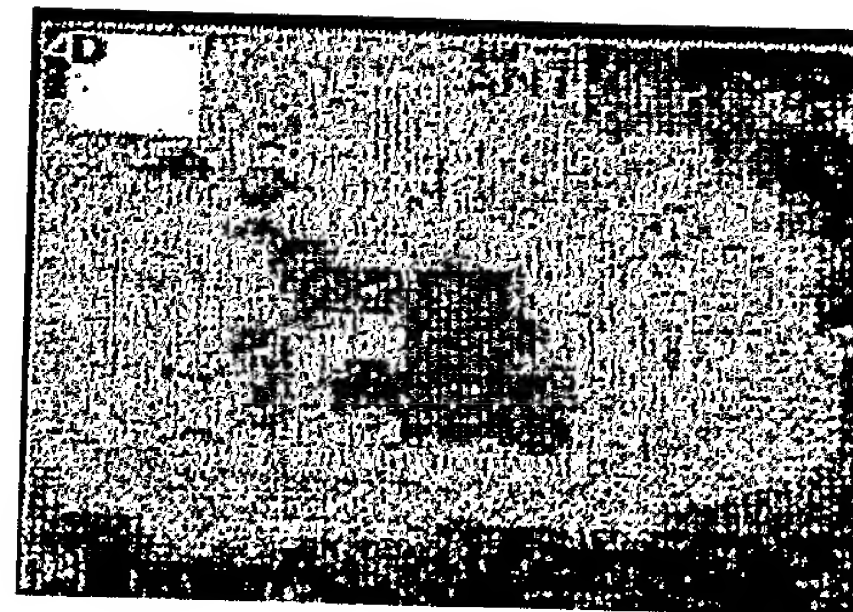


Fig. 29B

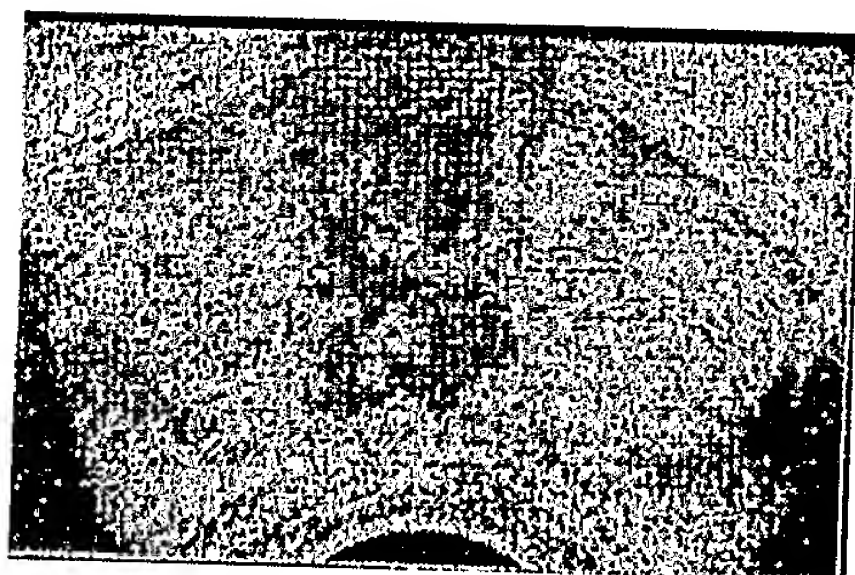


Fig. 29C

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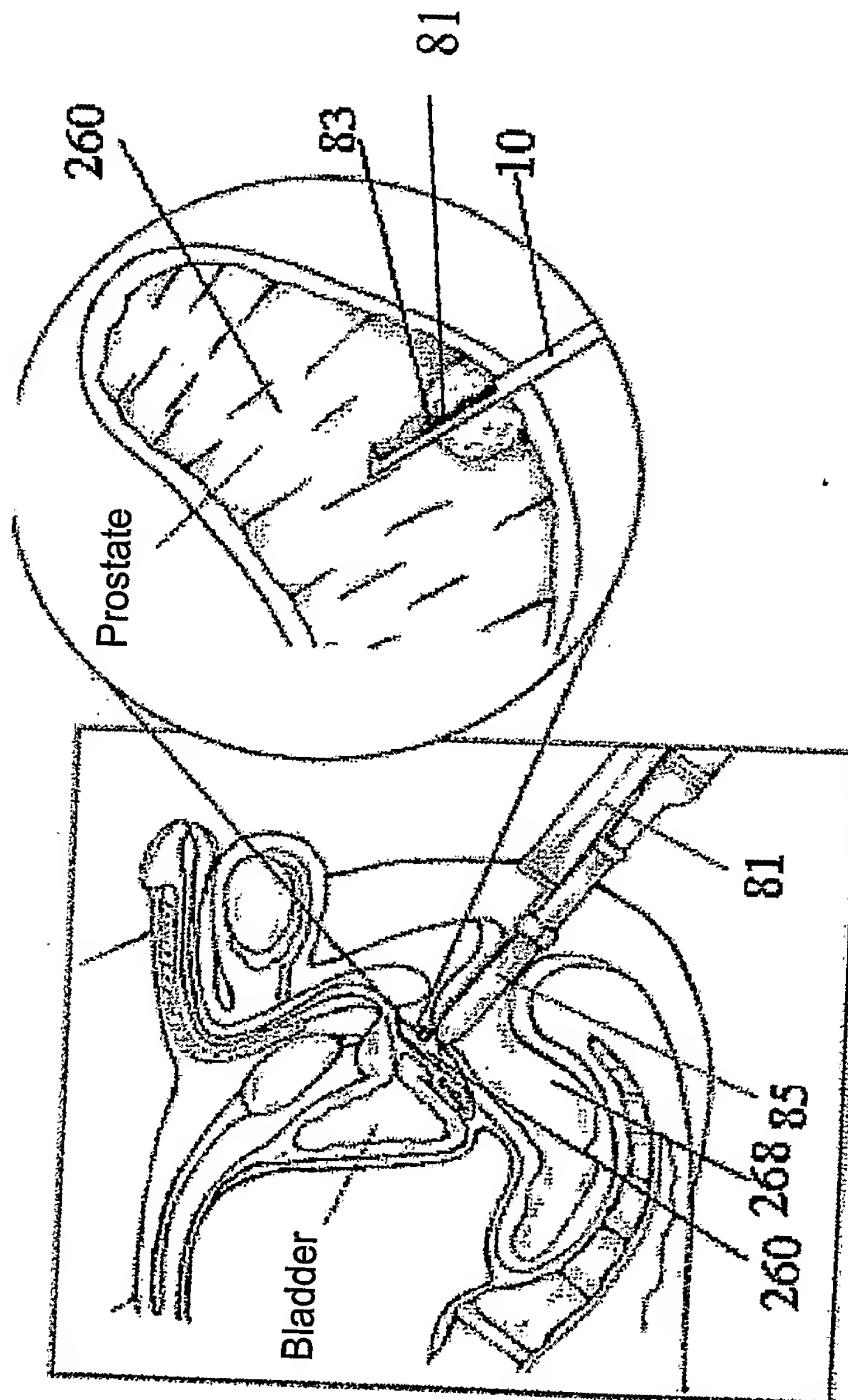


Fig. 30

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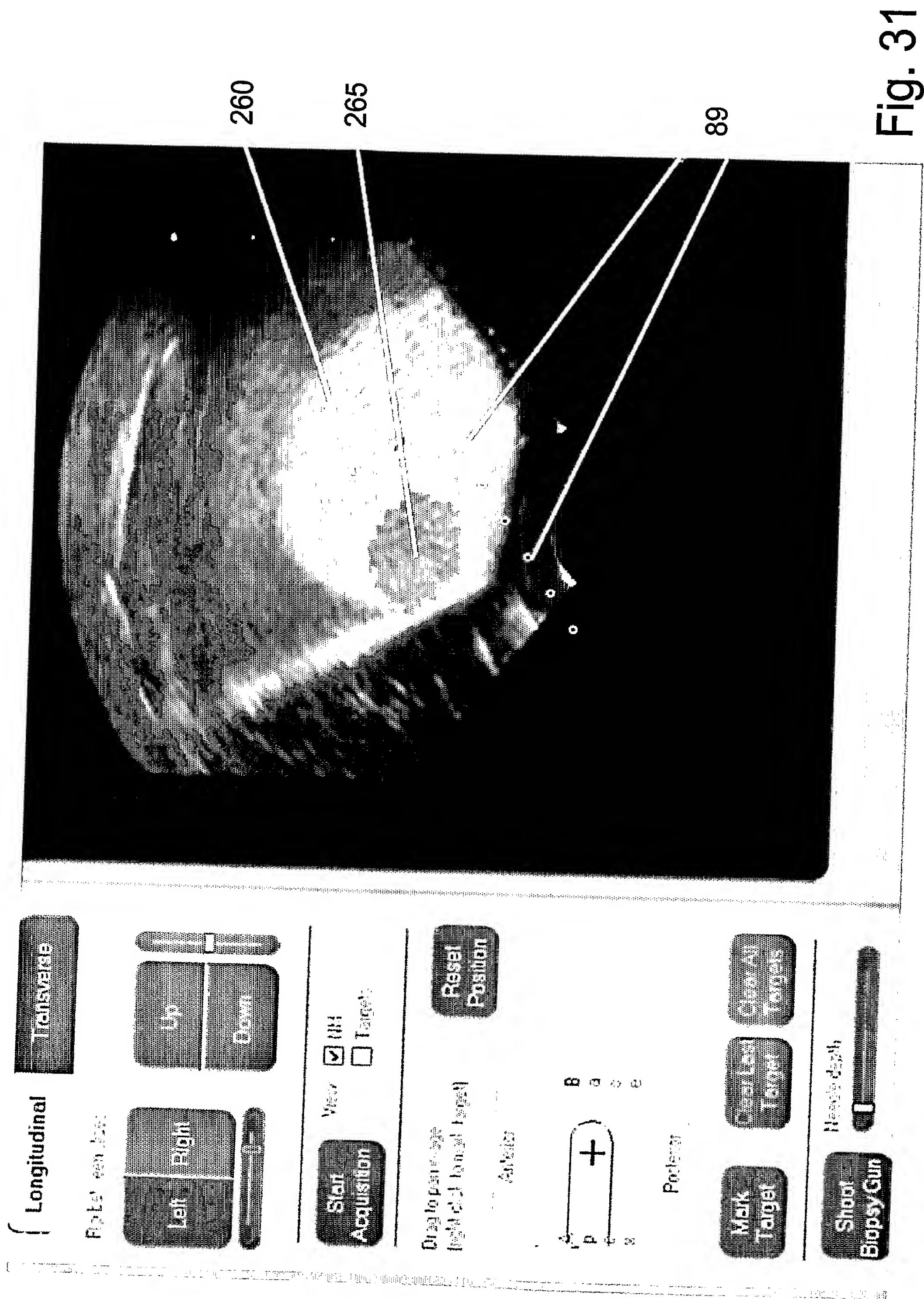


Fig. 31

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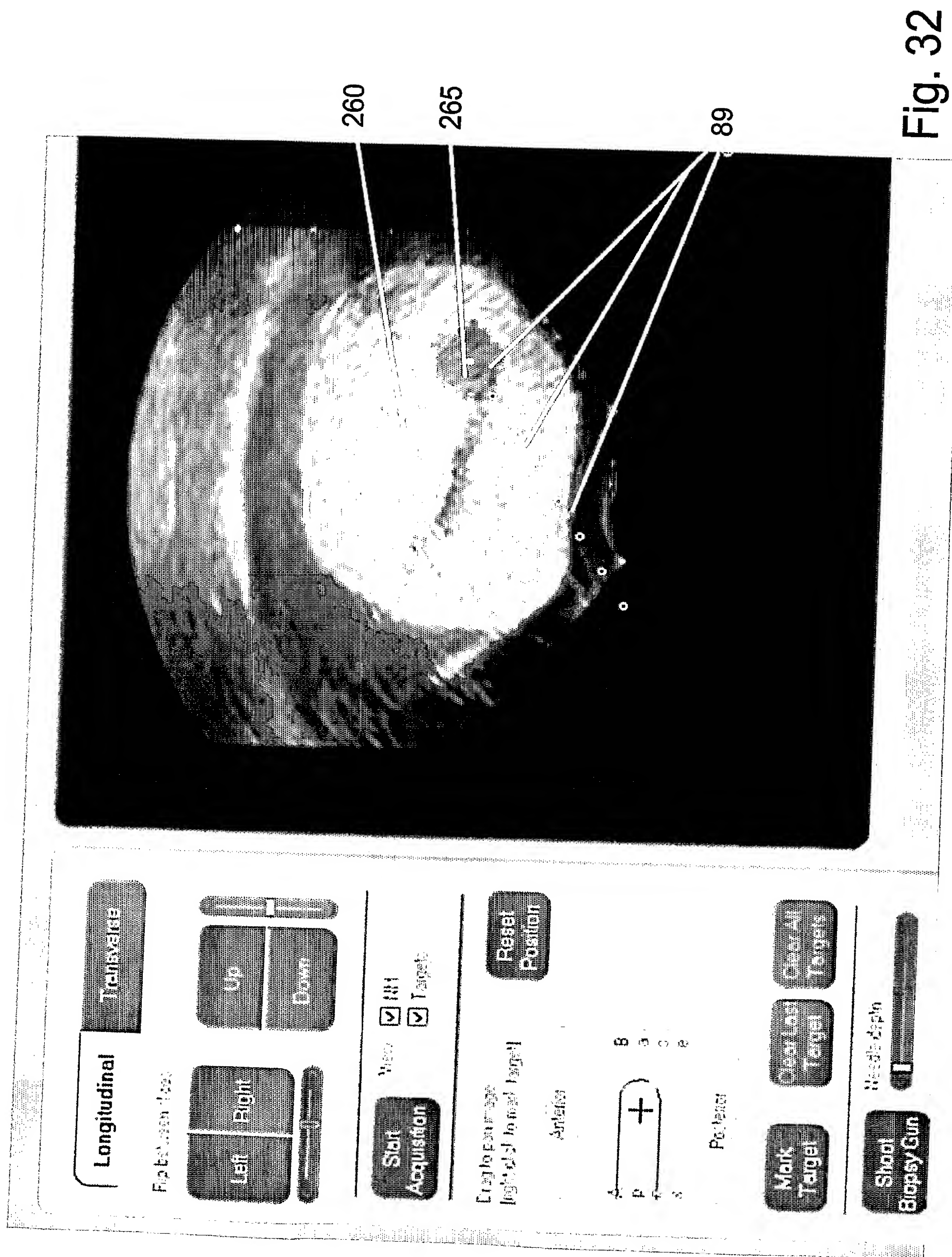


Fig. 32



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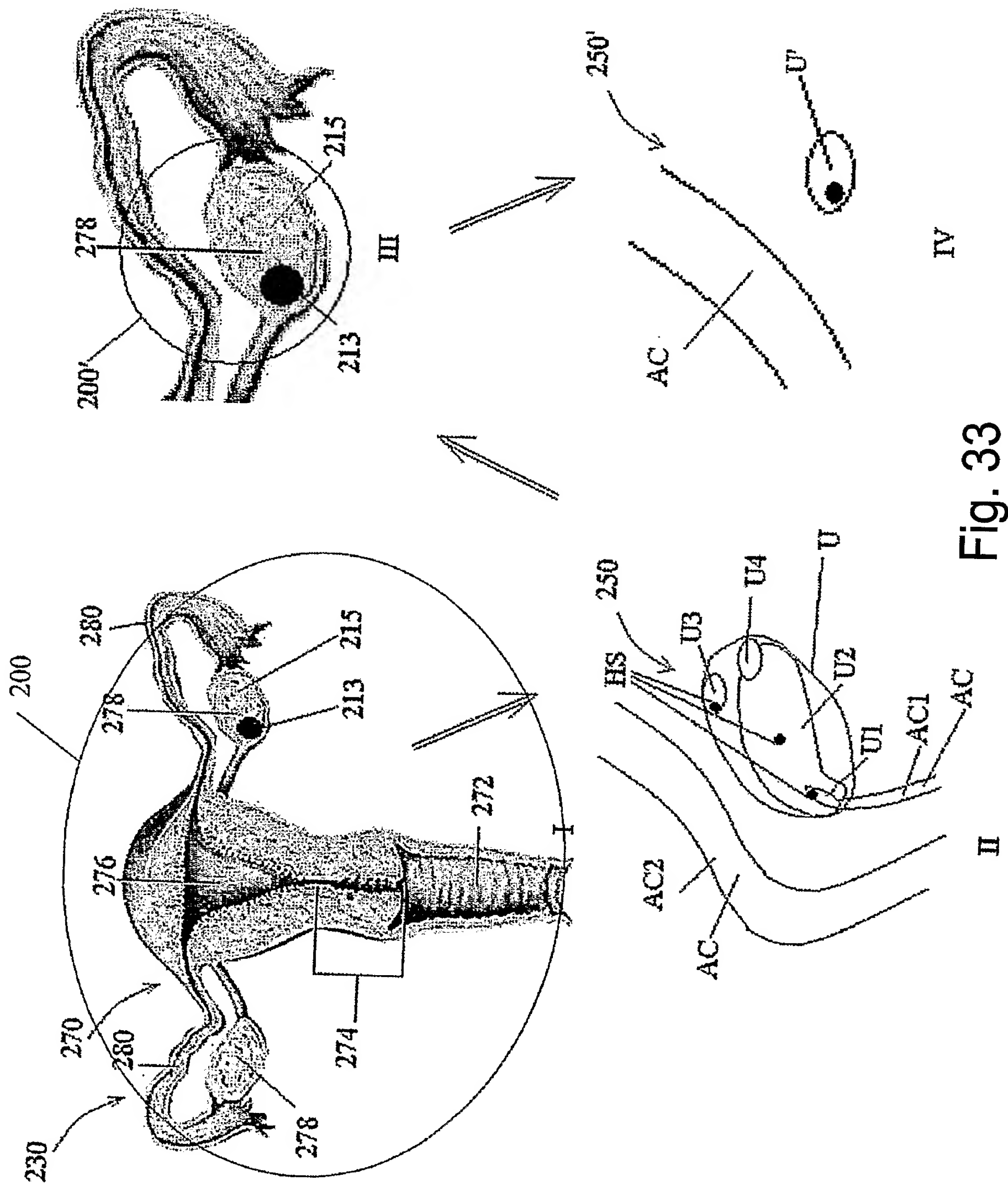


Fig. 33

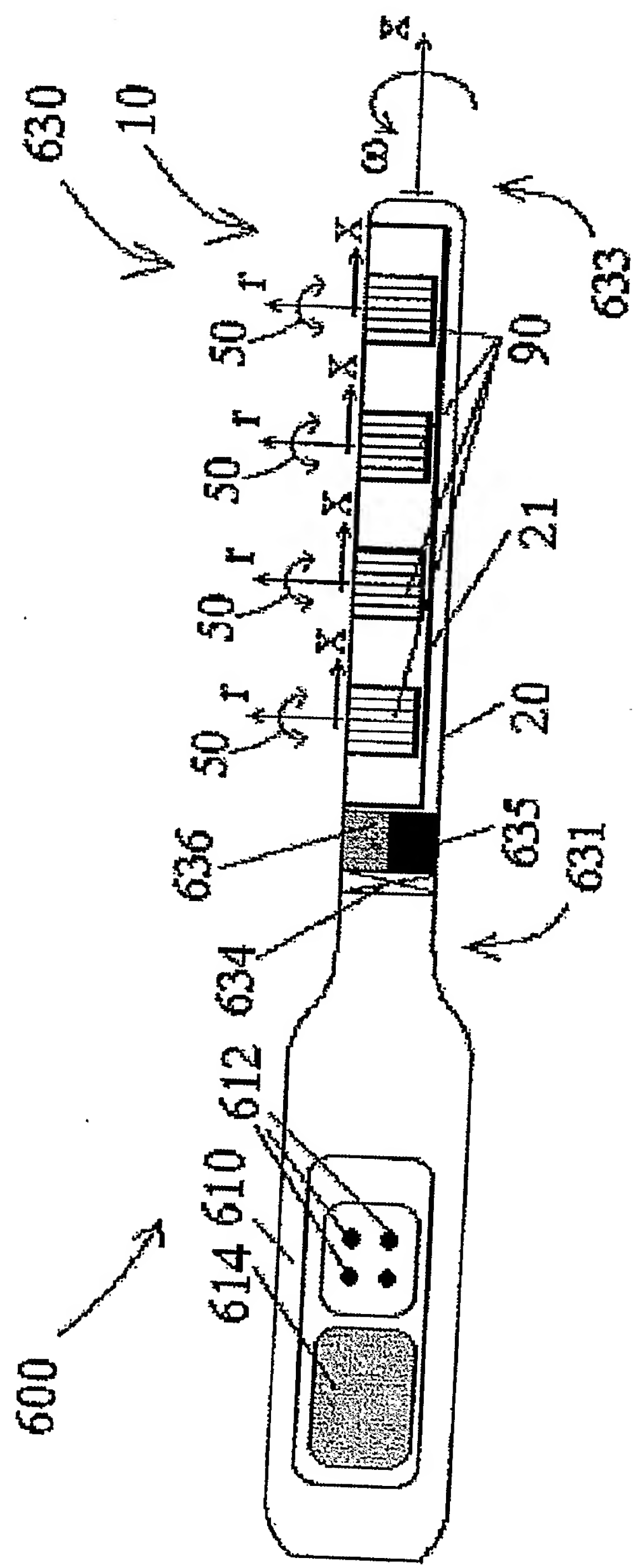


Fig. 34A

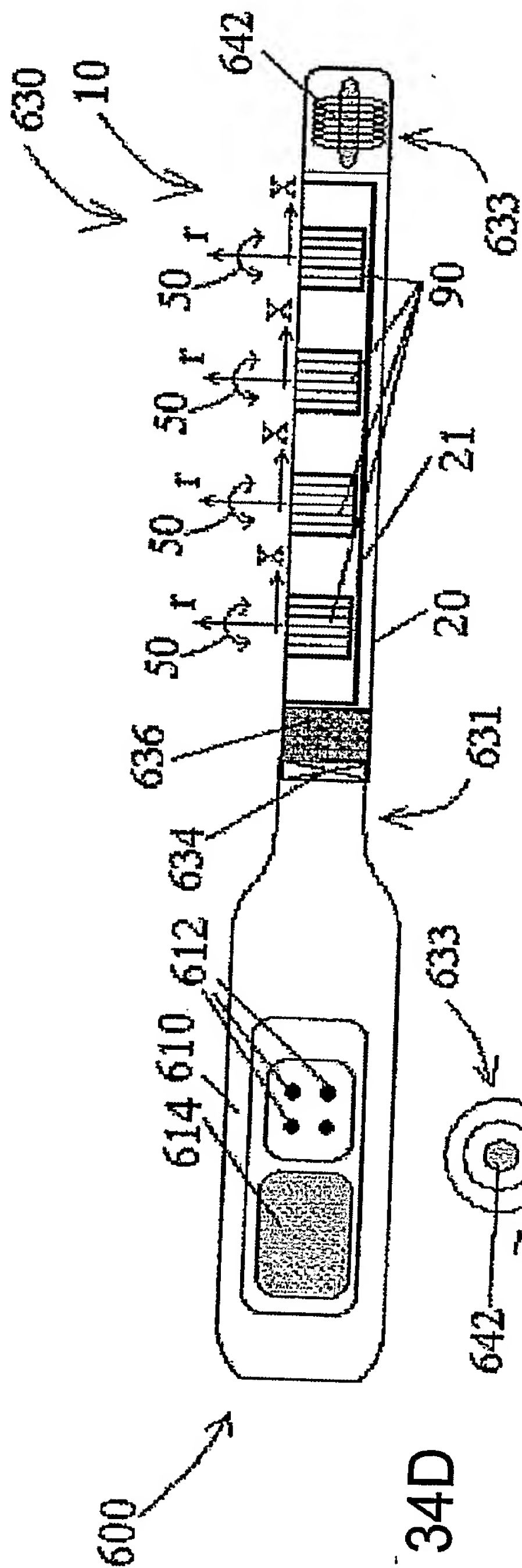


Fig. 34D

Fig. 34E

Figure

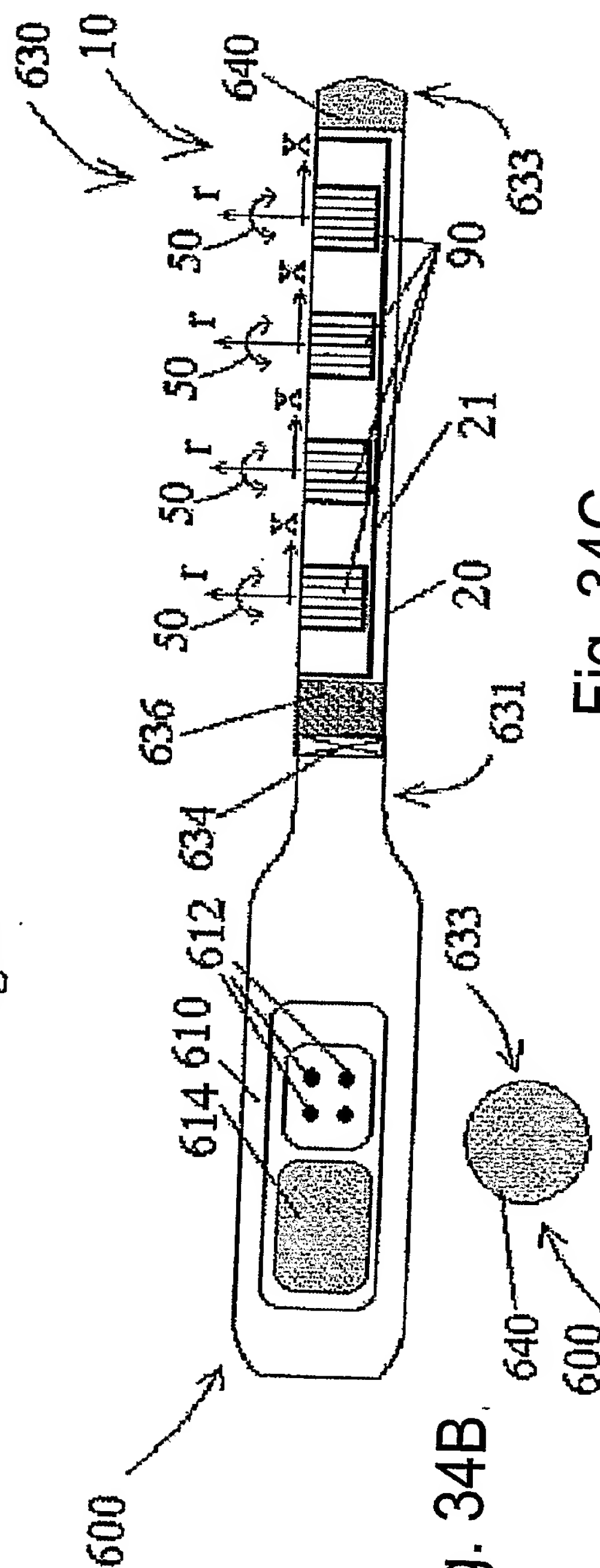


Fig. 34B

Fig. 34C



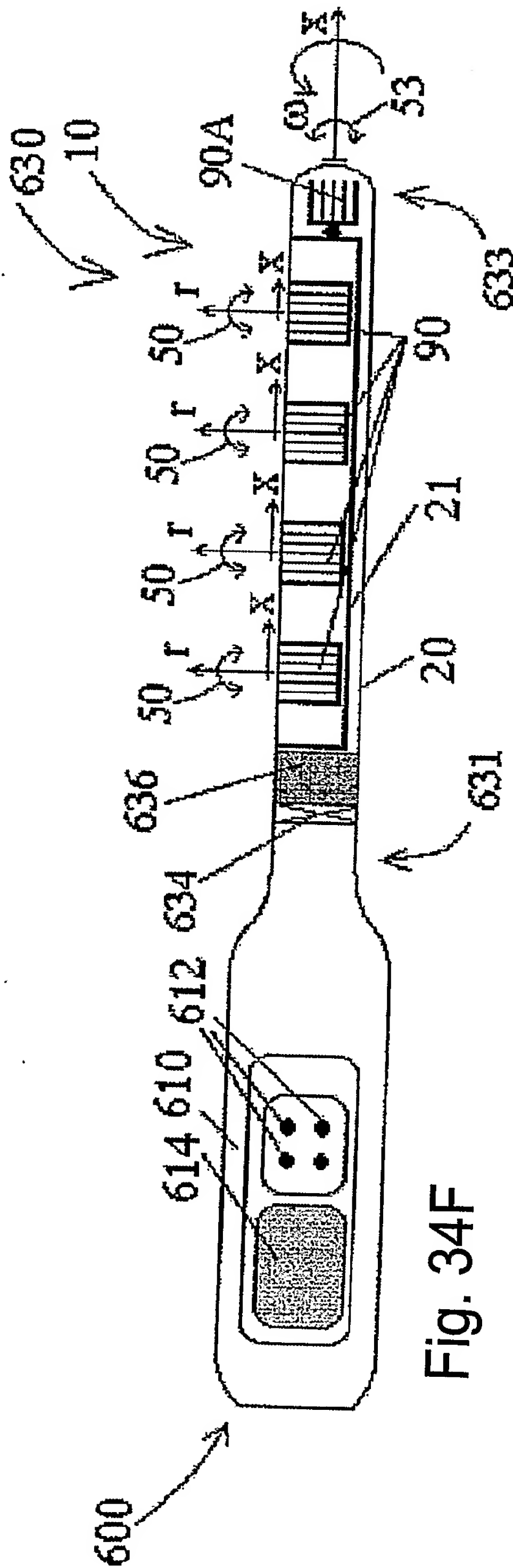


Fig. 34F

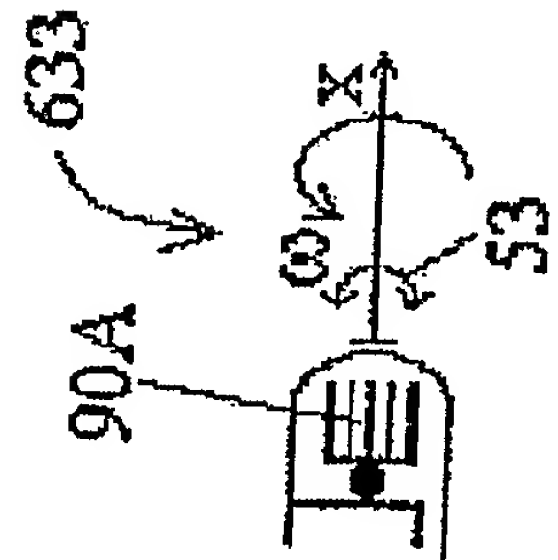


Fig. 34G

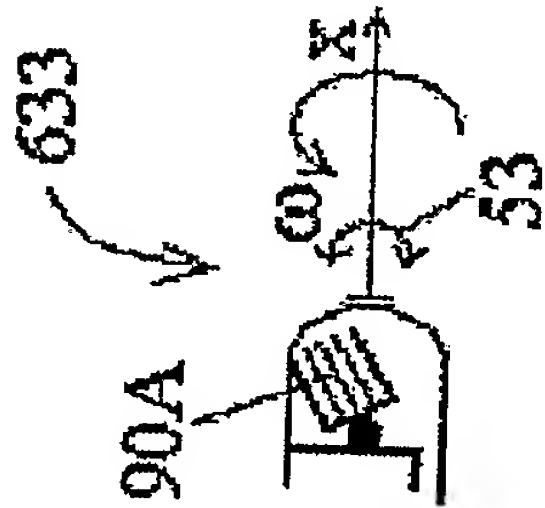


Fig. 34H

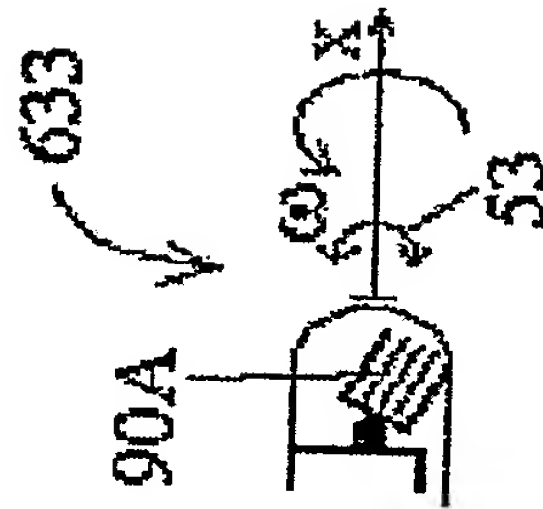


Fig. 34I

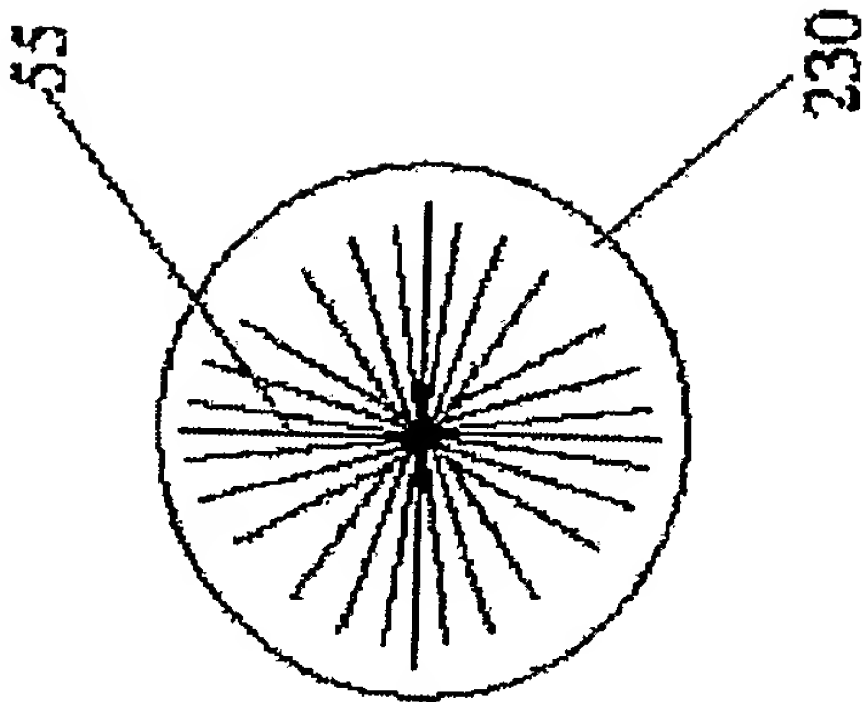


Fig. 34K

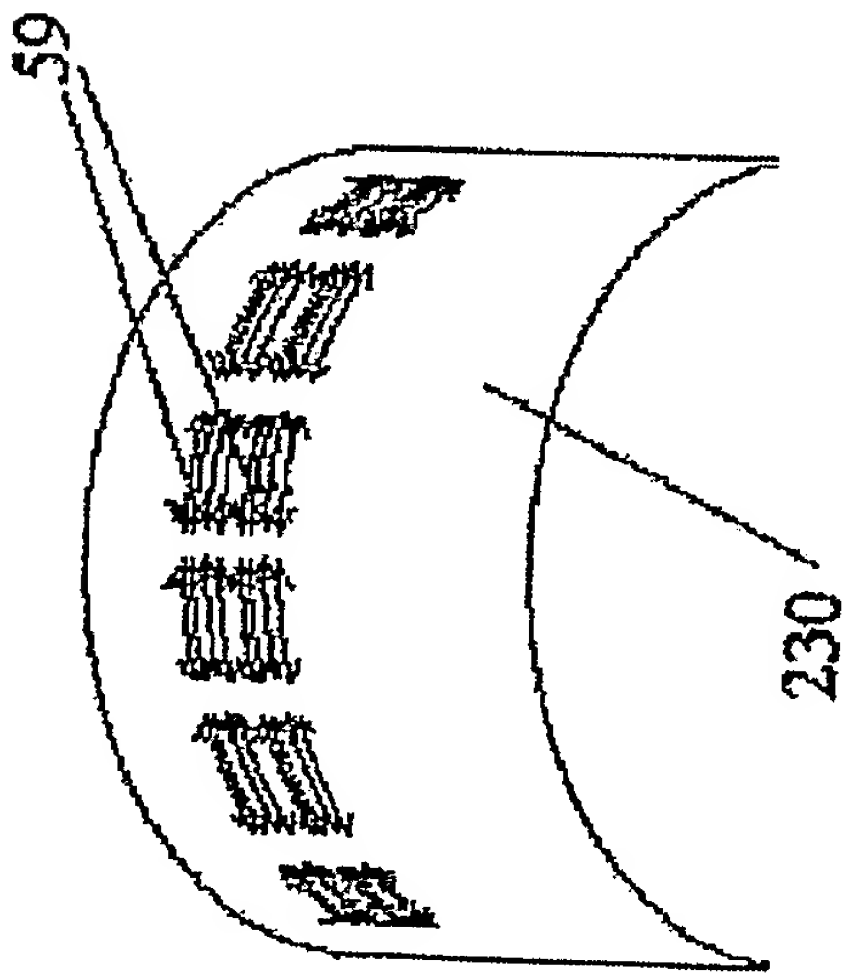
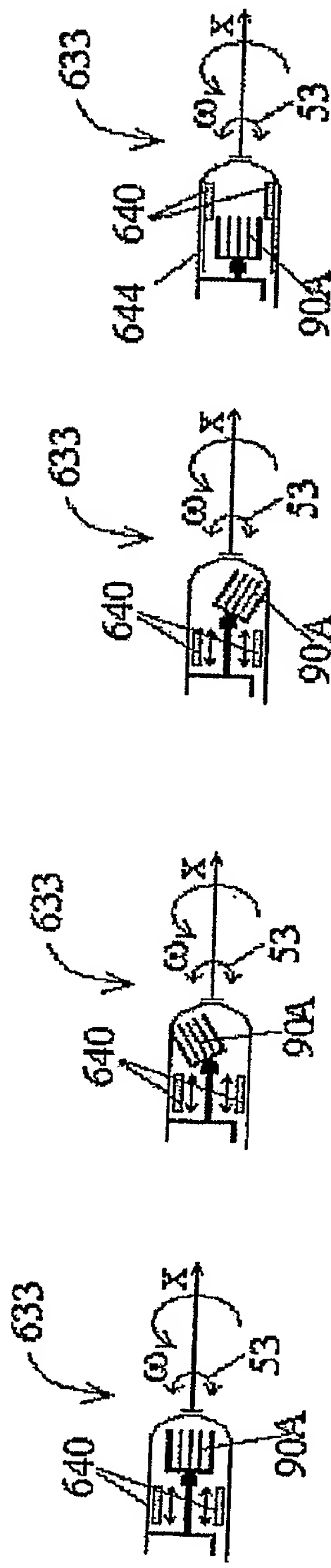
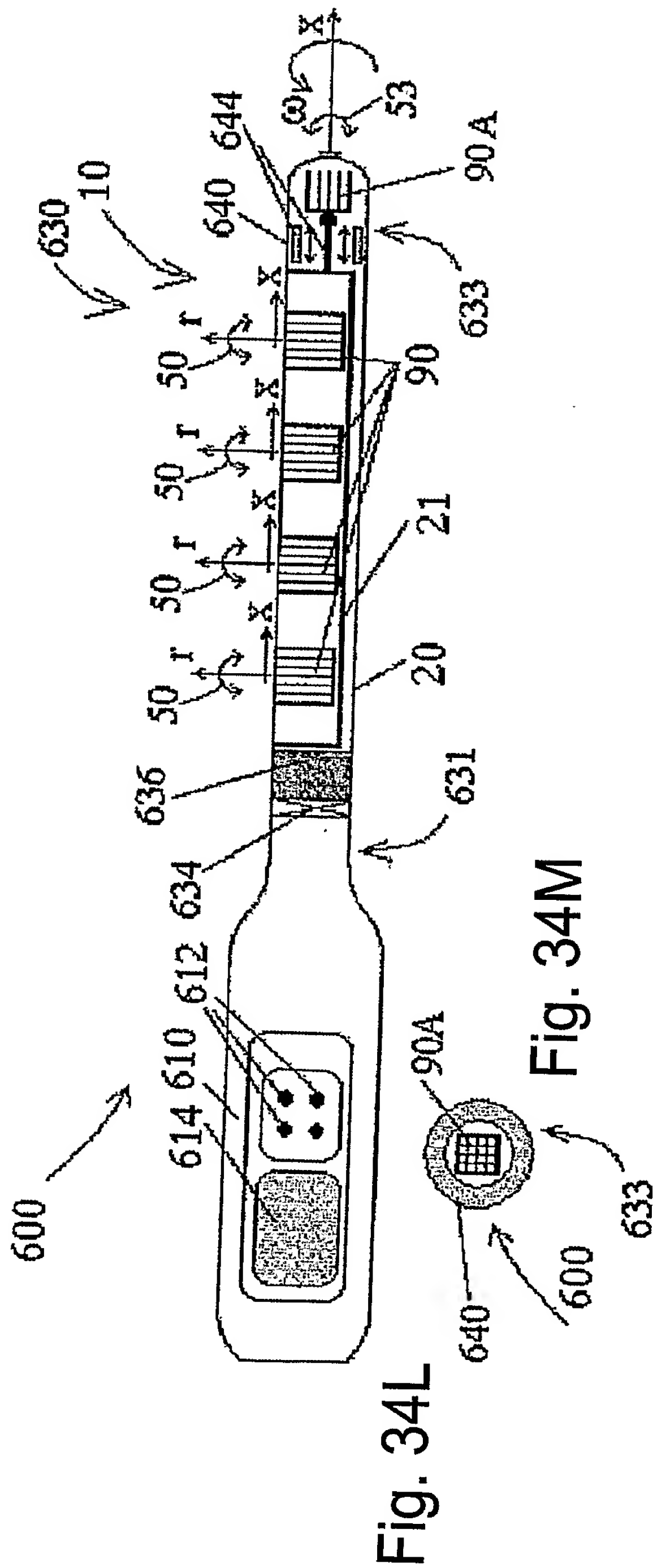
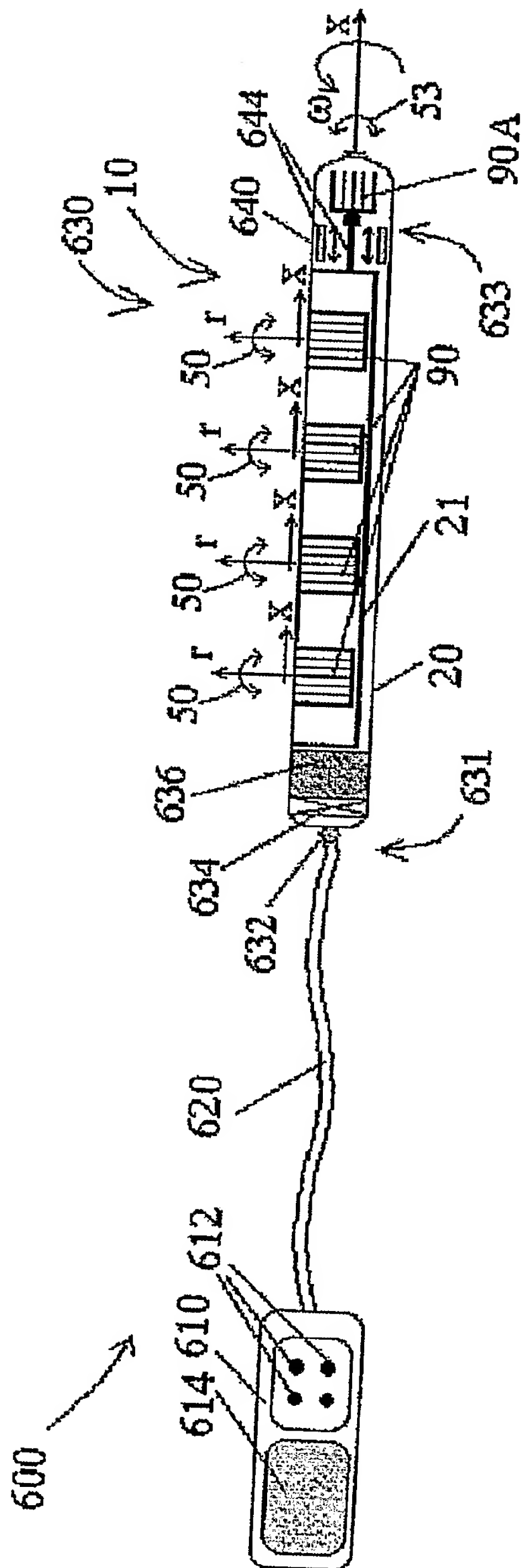


Fig. 34J





**Fig. 34R**

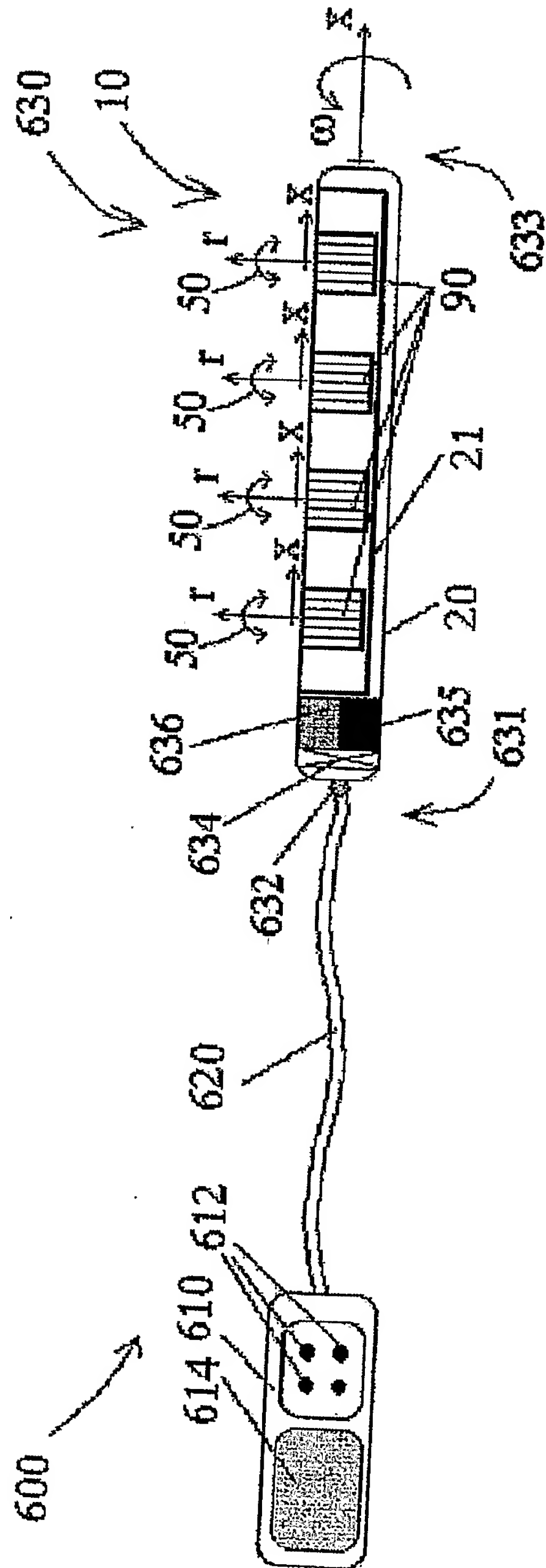
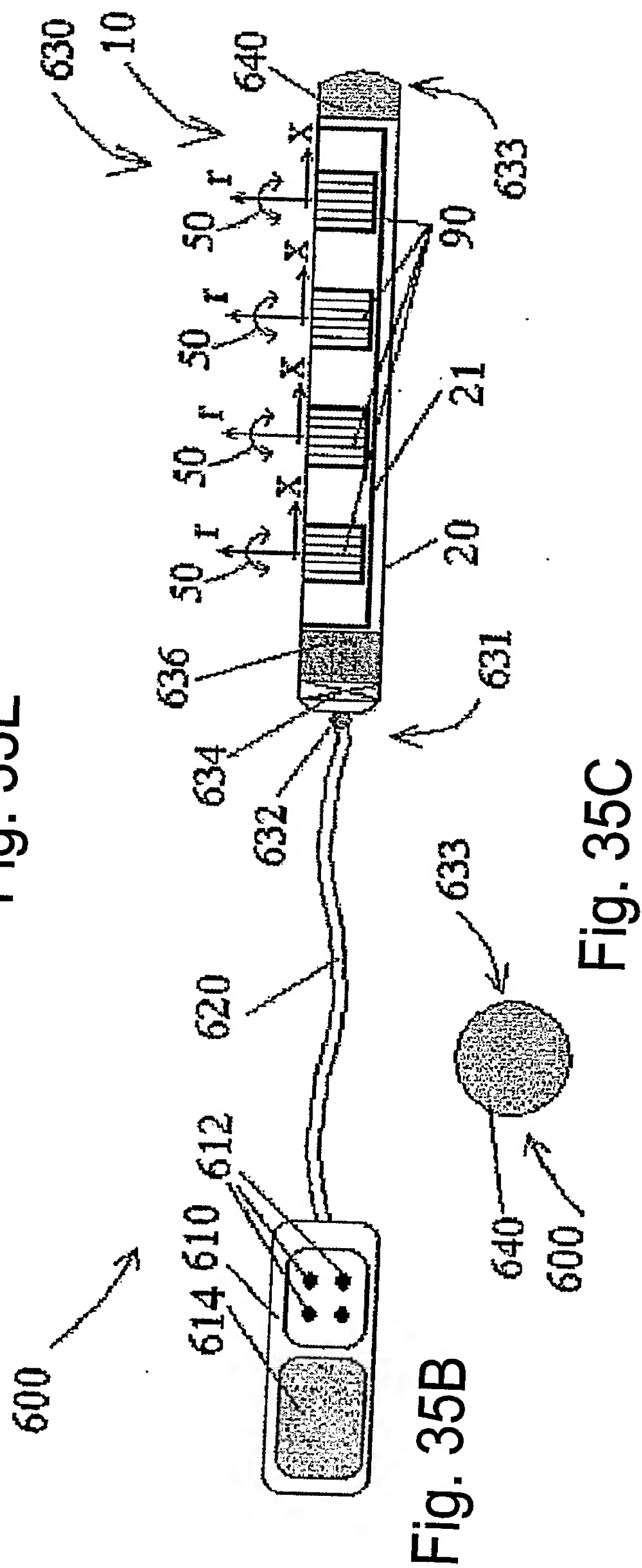
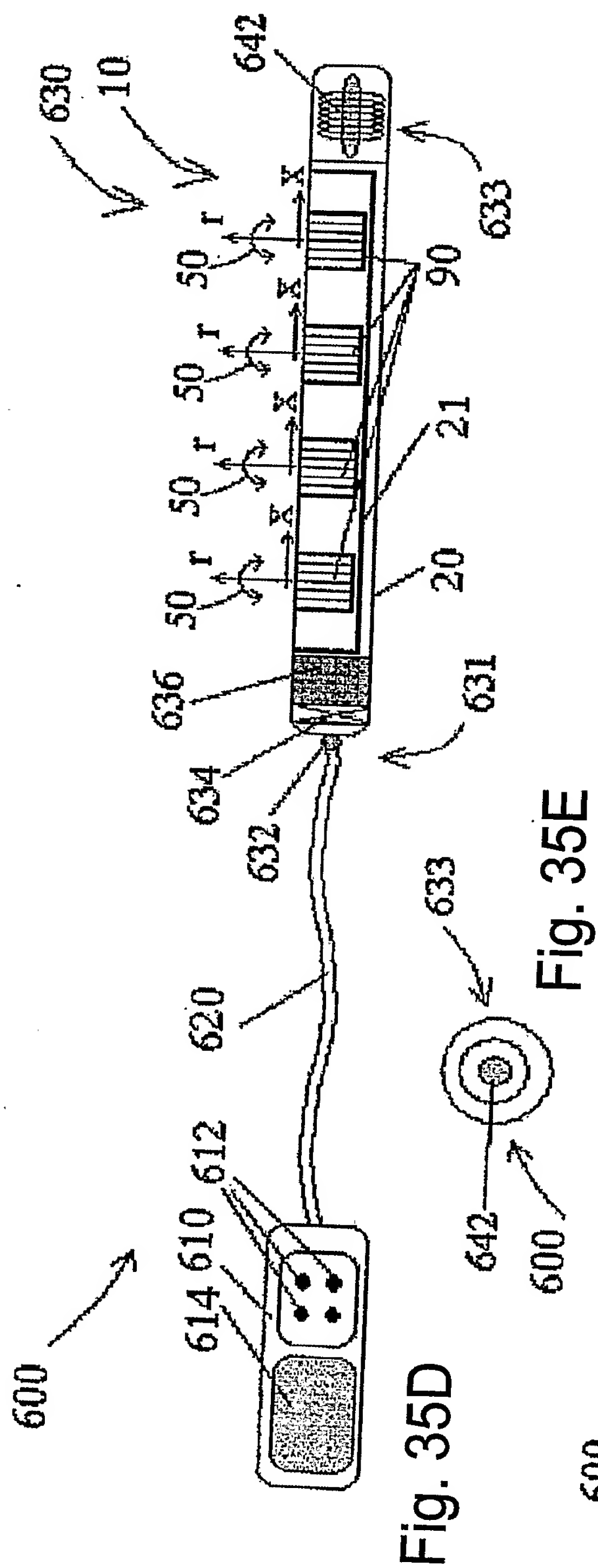


Fig. 35A



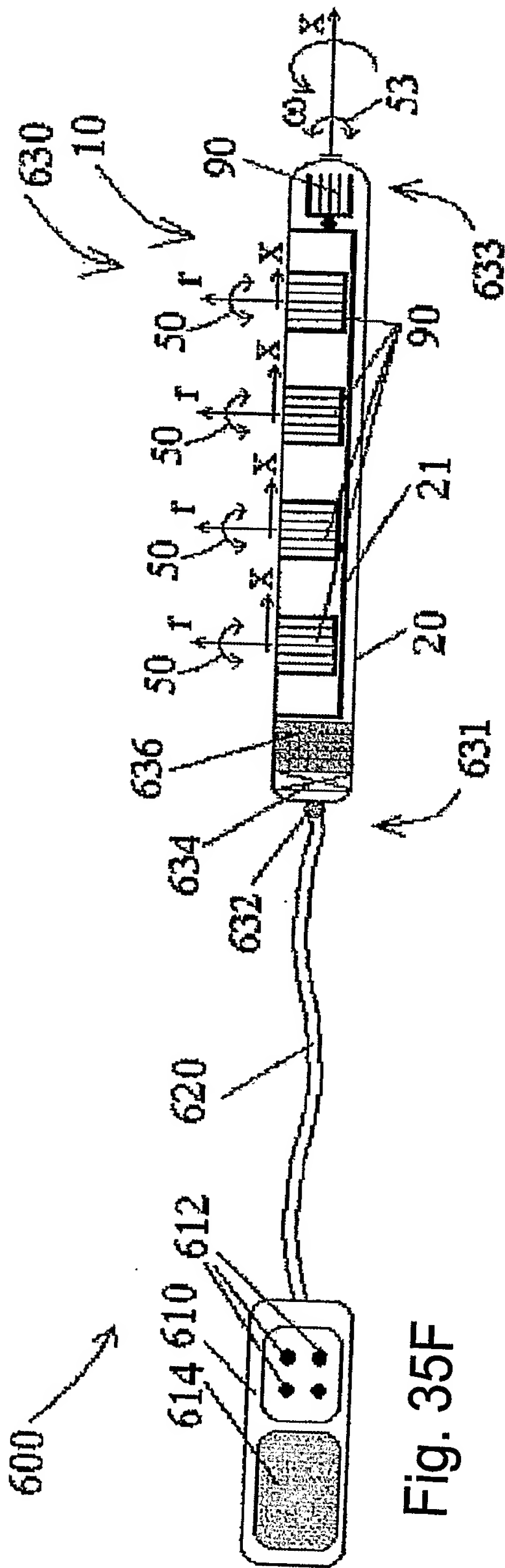


Fig. 35F

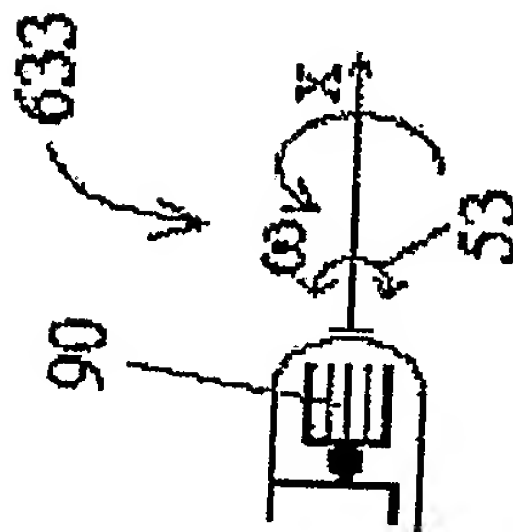


Fig. 35G

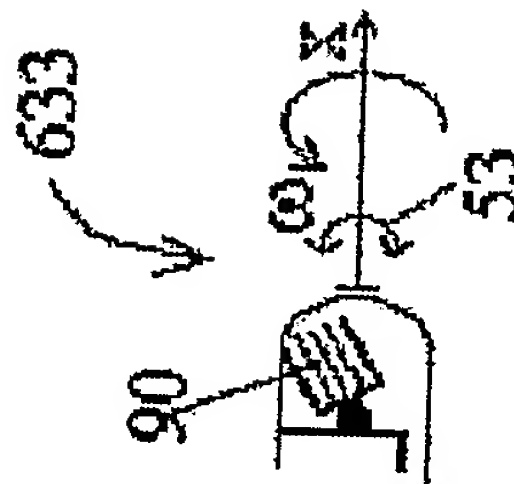


Fig. 35H

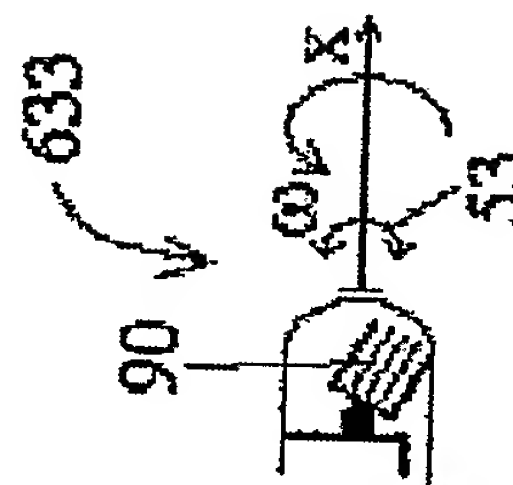


Fig. 35I



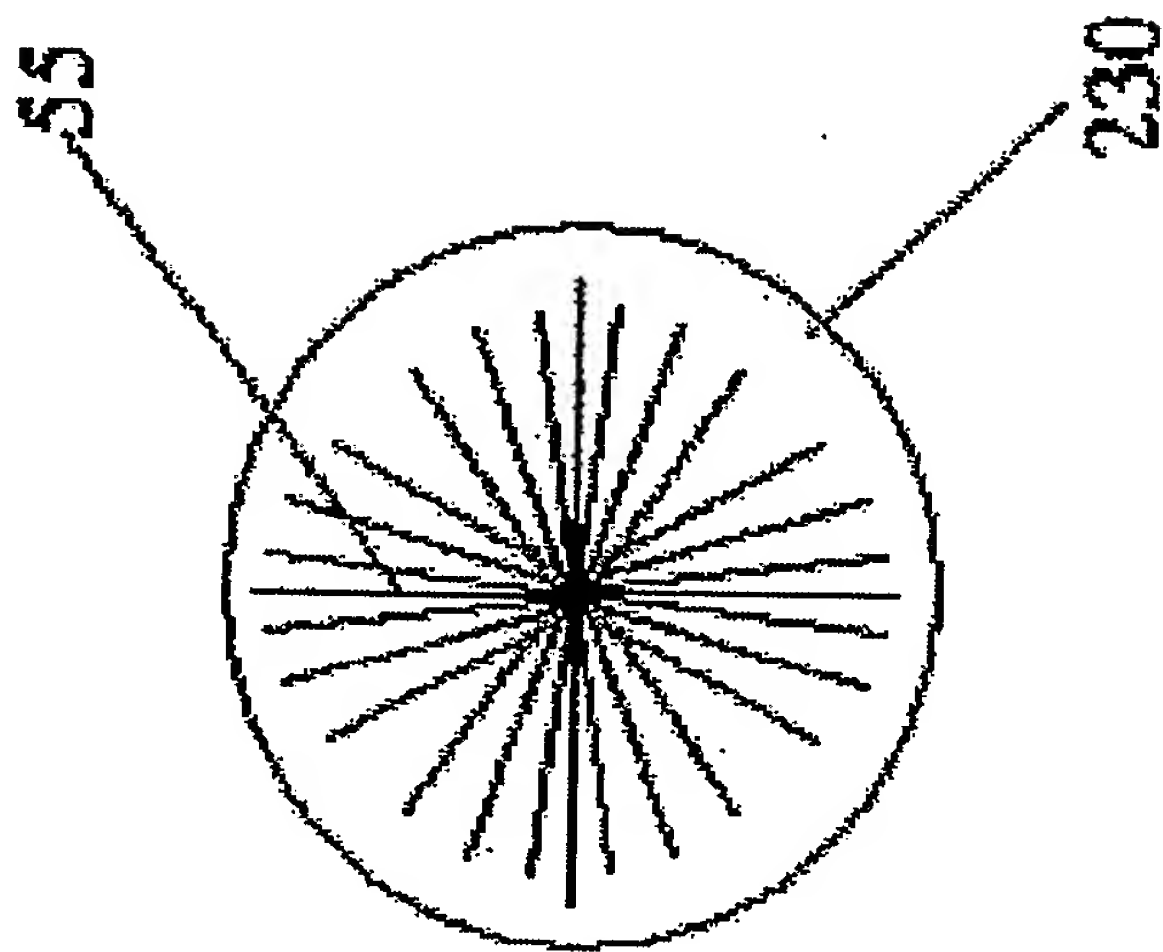


Fig. 35K

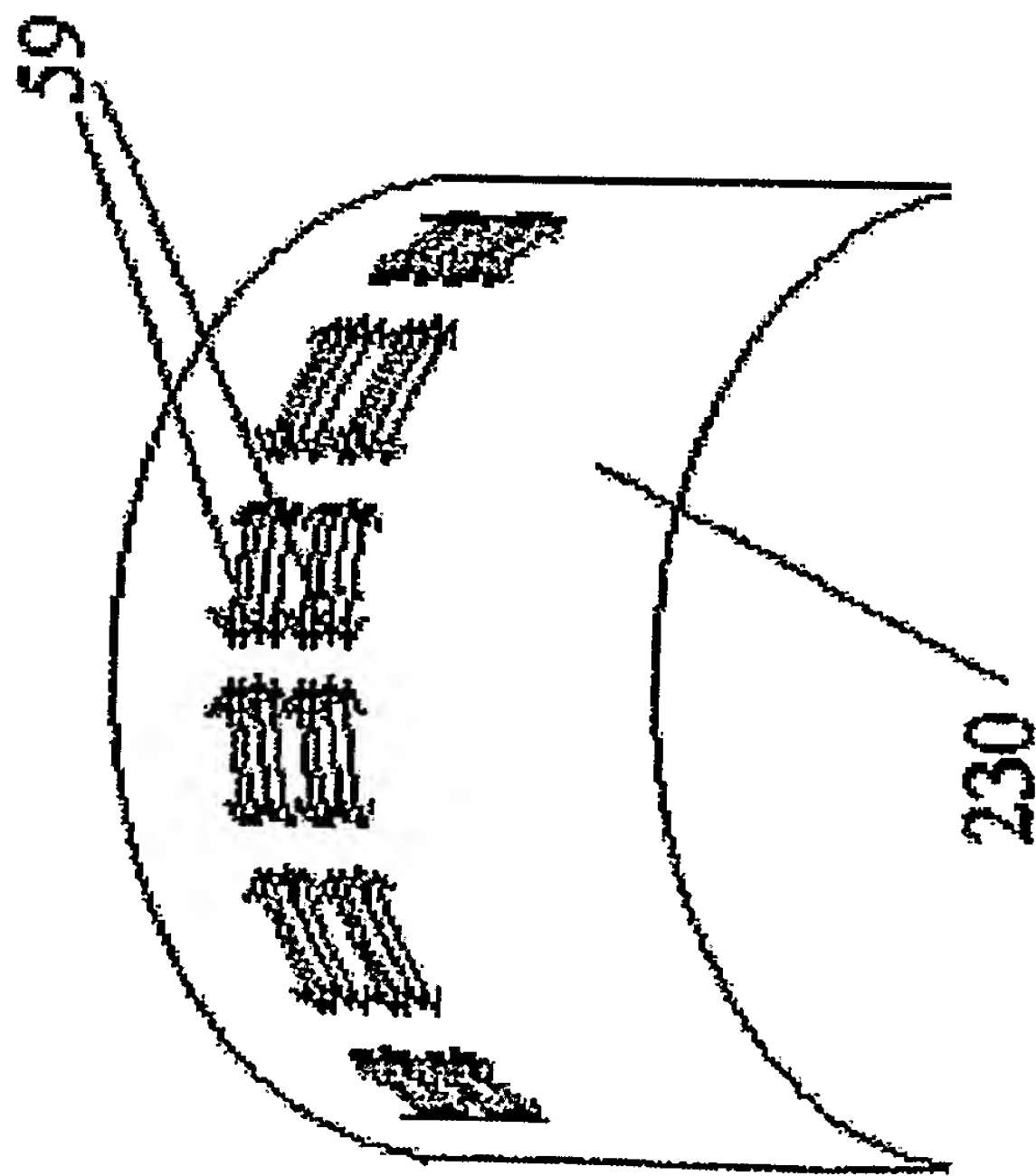
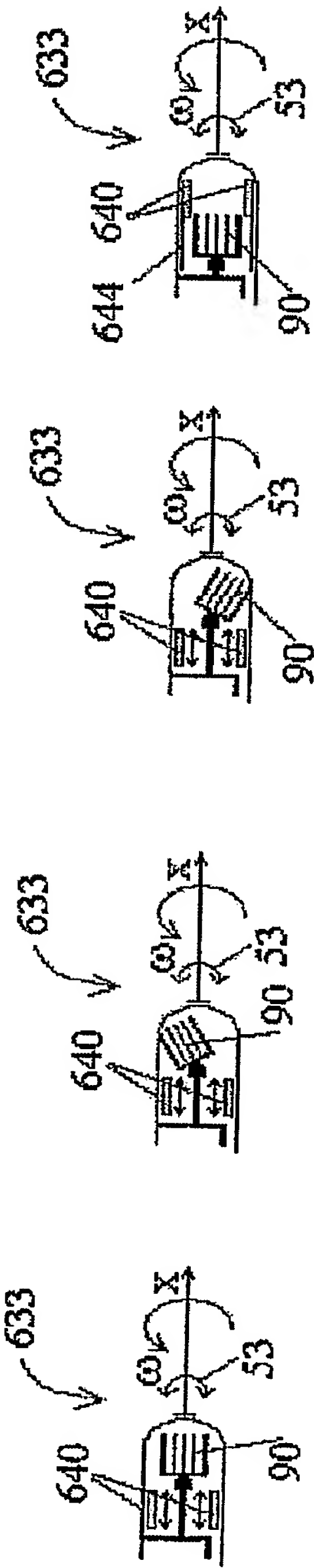
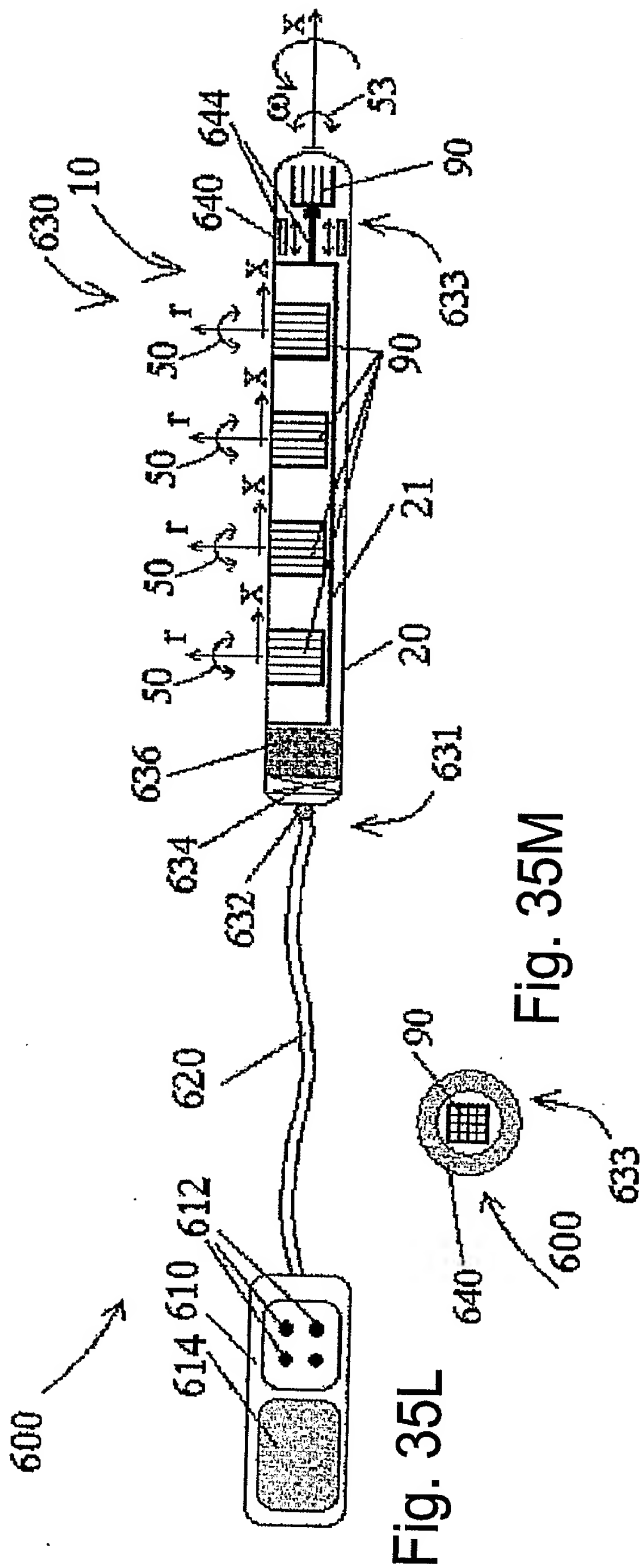


Fig. 35J



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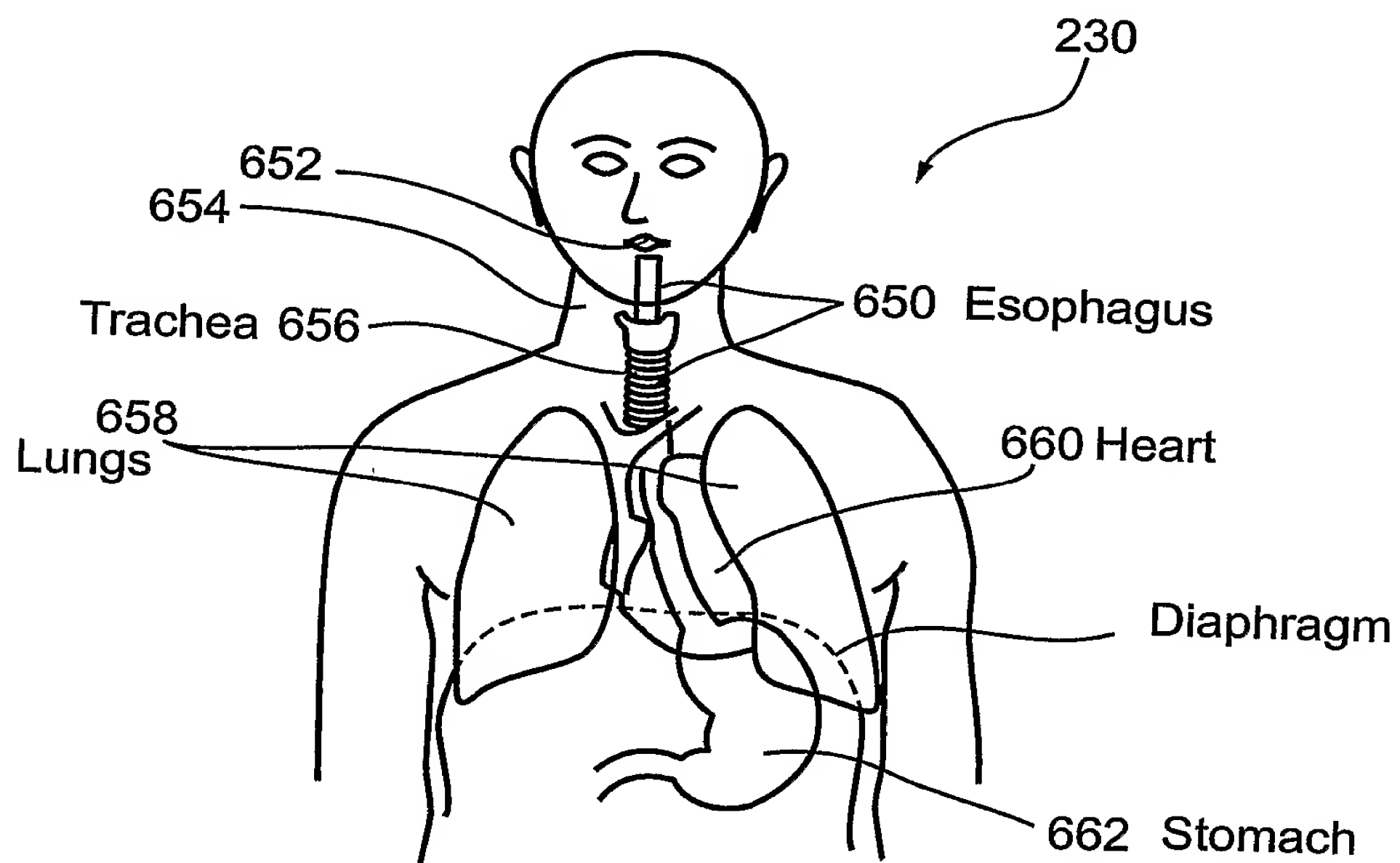


Fig. 36A

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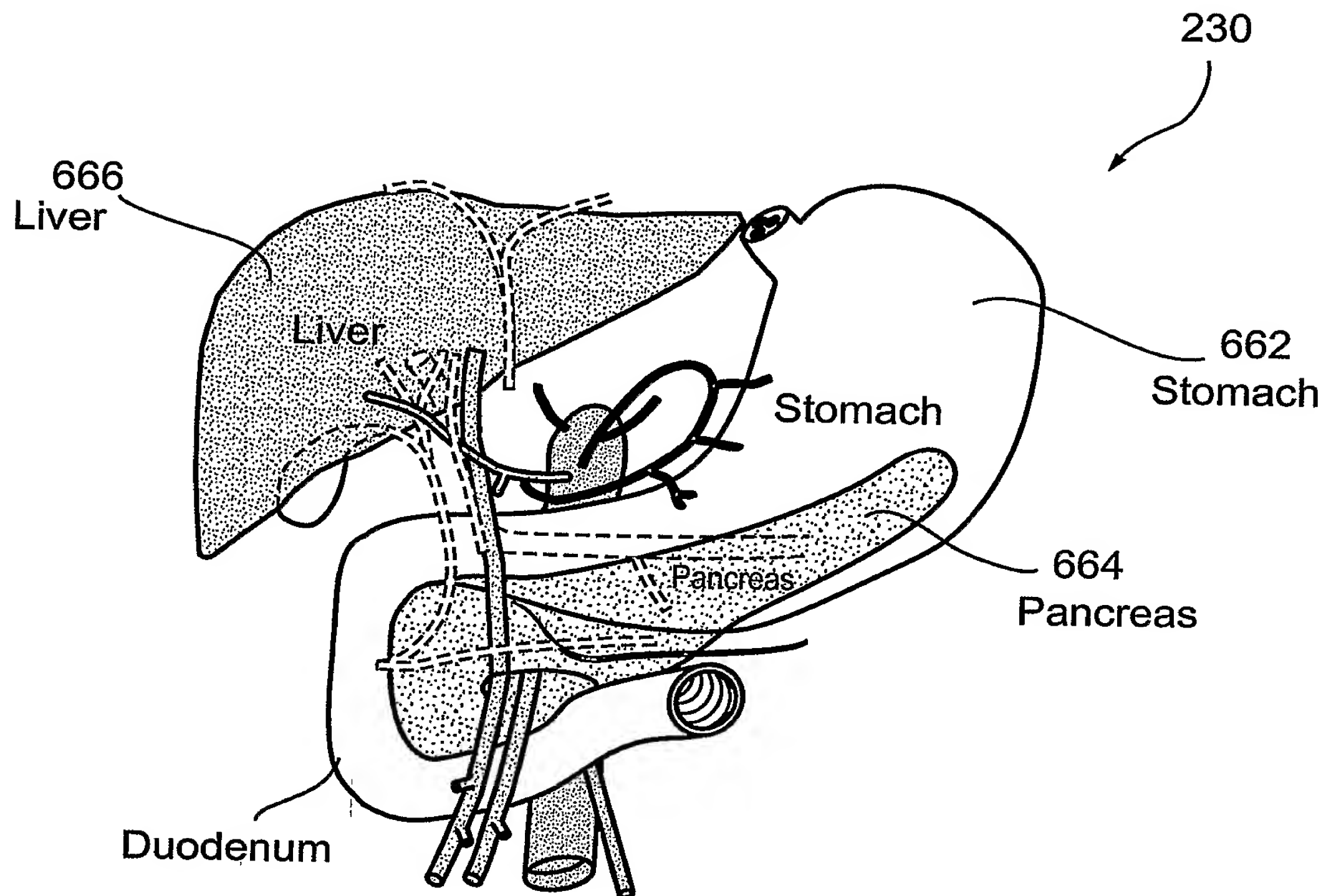


Fig. 36B

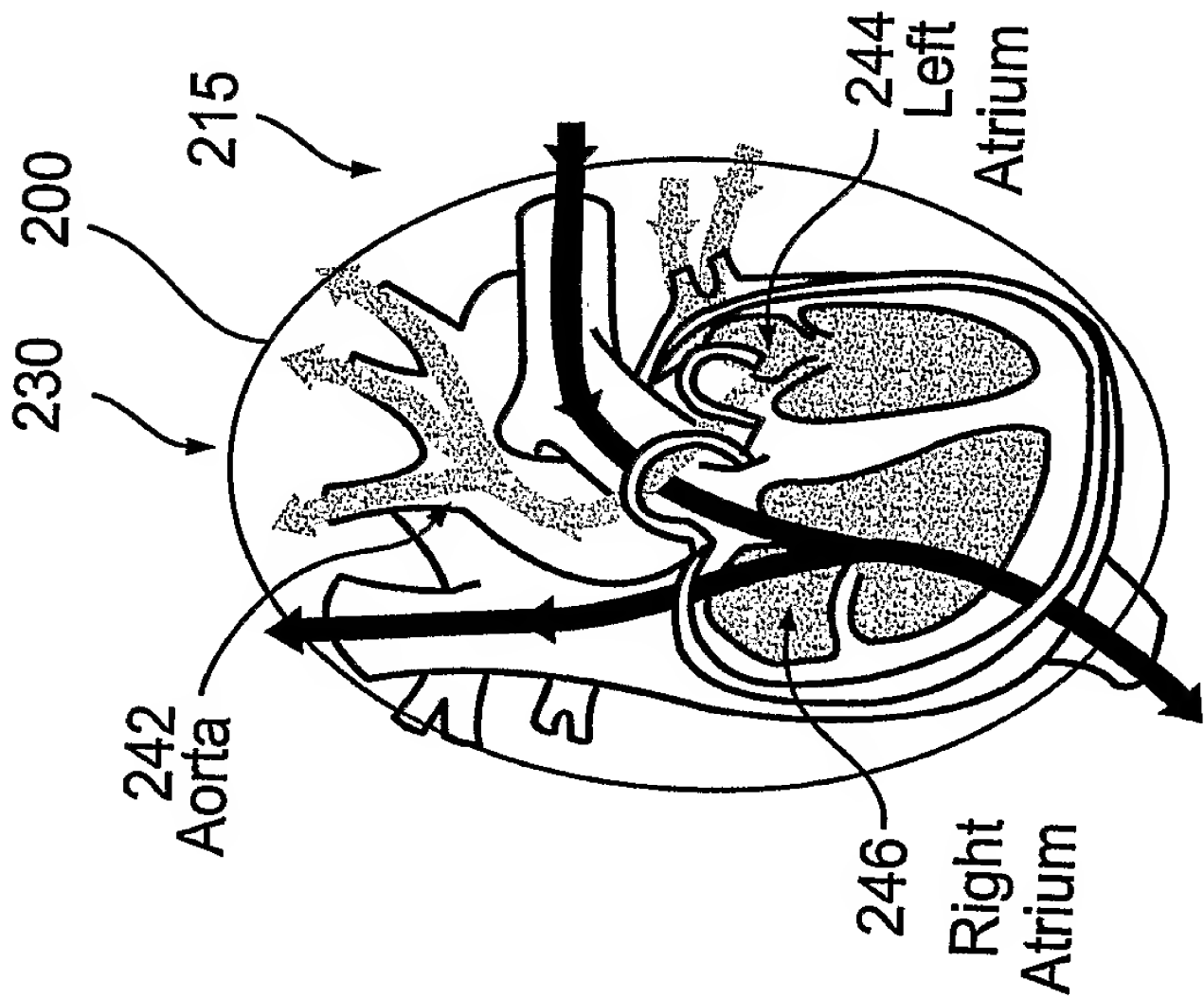


Fig. 37

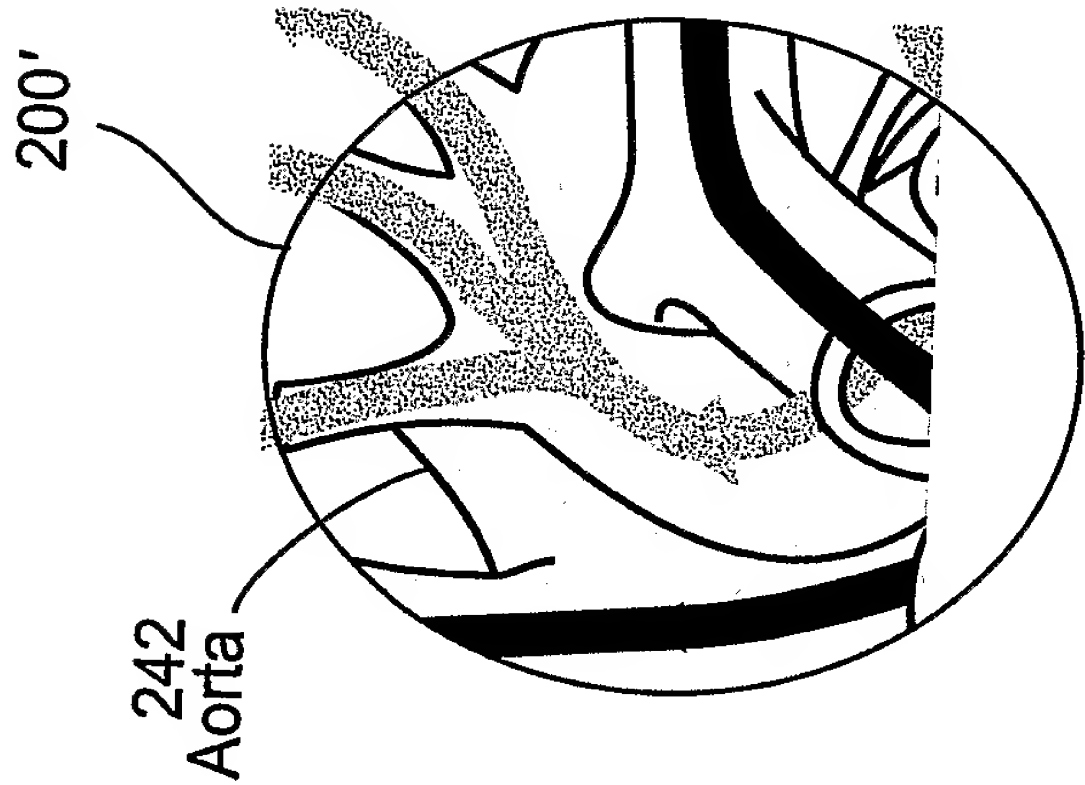


Fig. 38

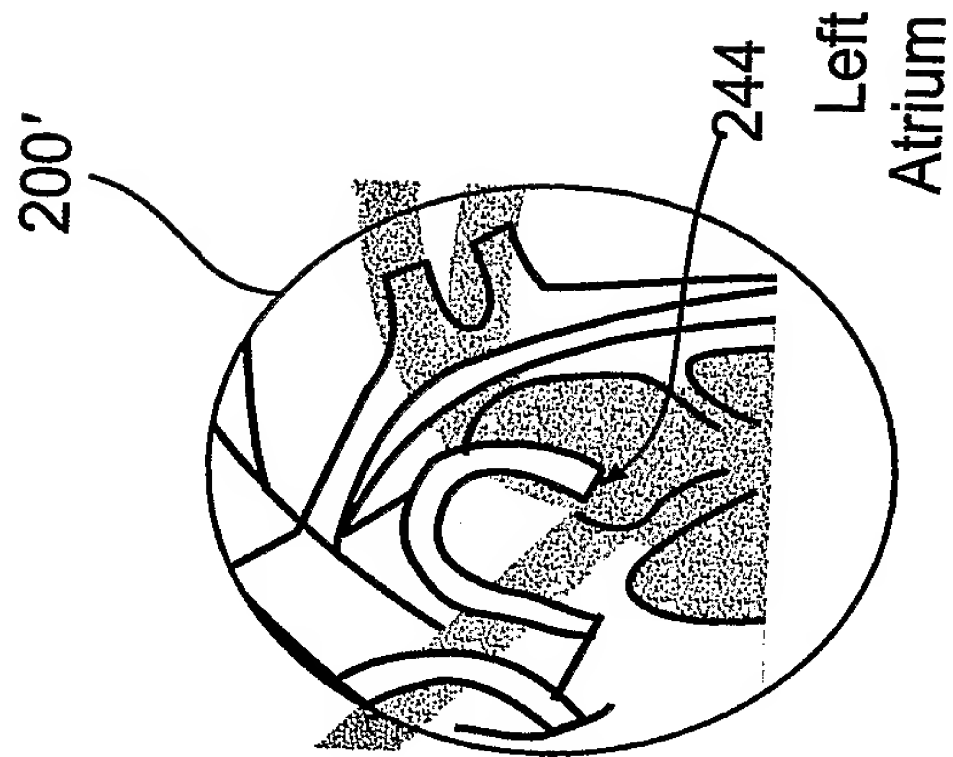


Fig. 39

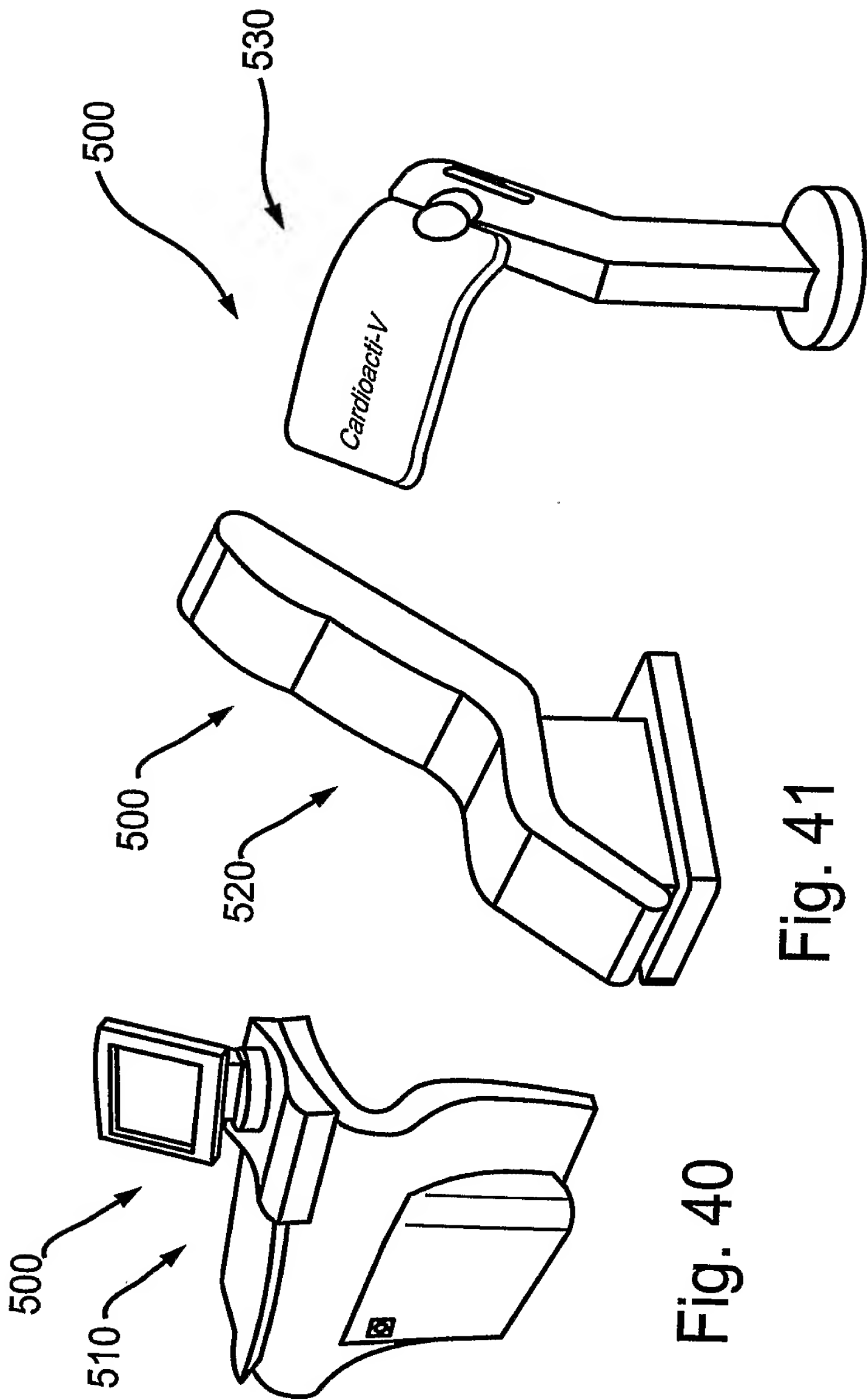


Fig. 42

Fig. 41

Fig. 40

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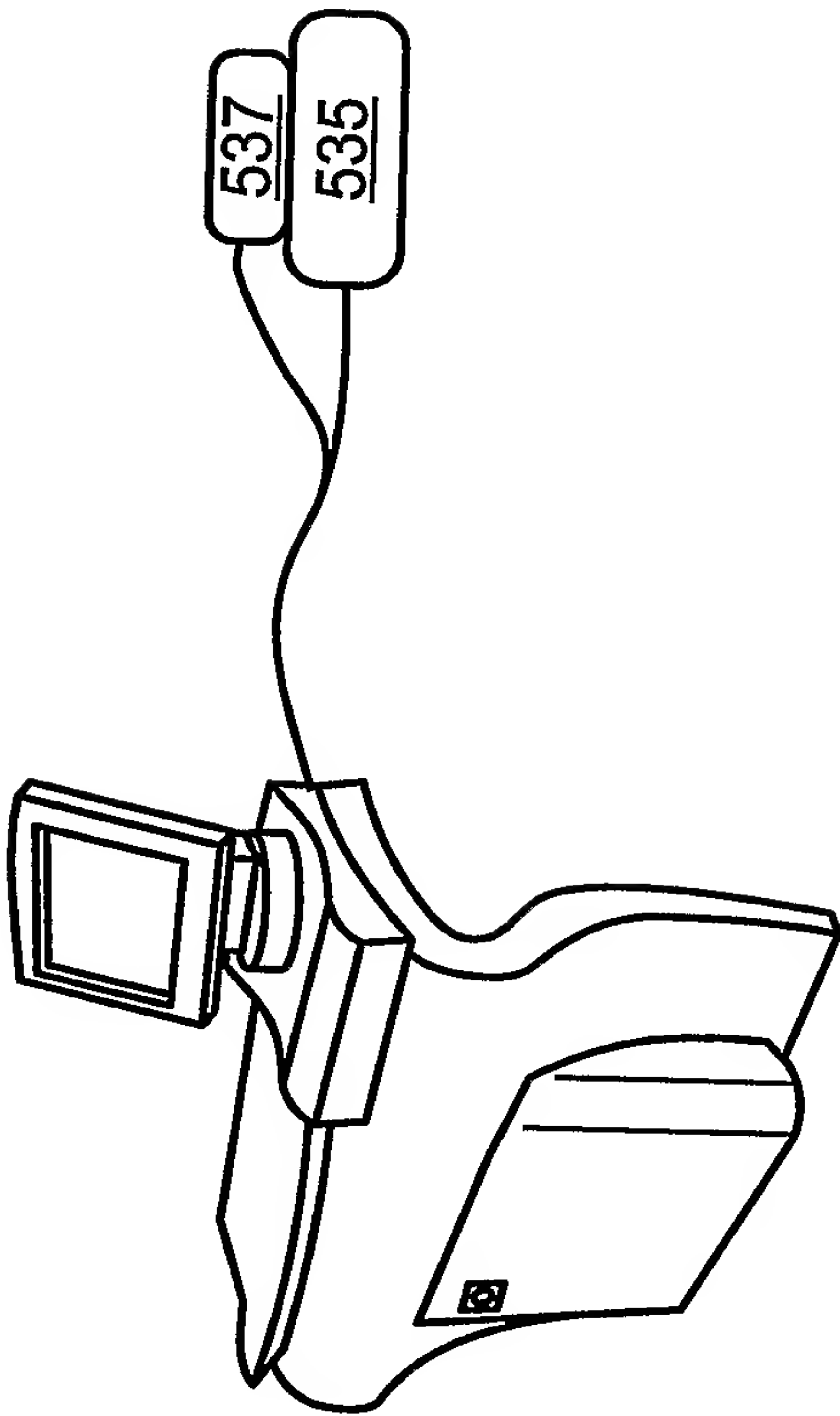


Fig. 43

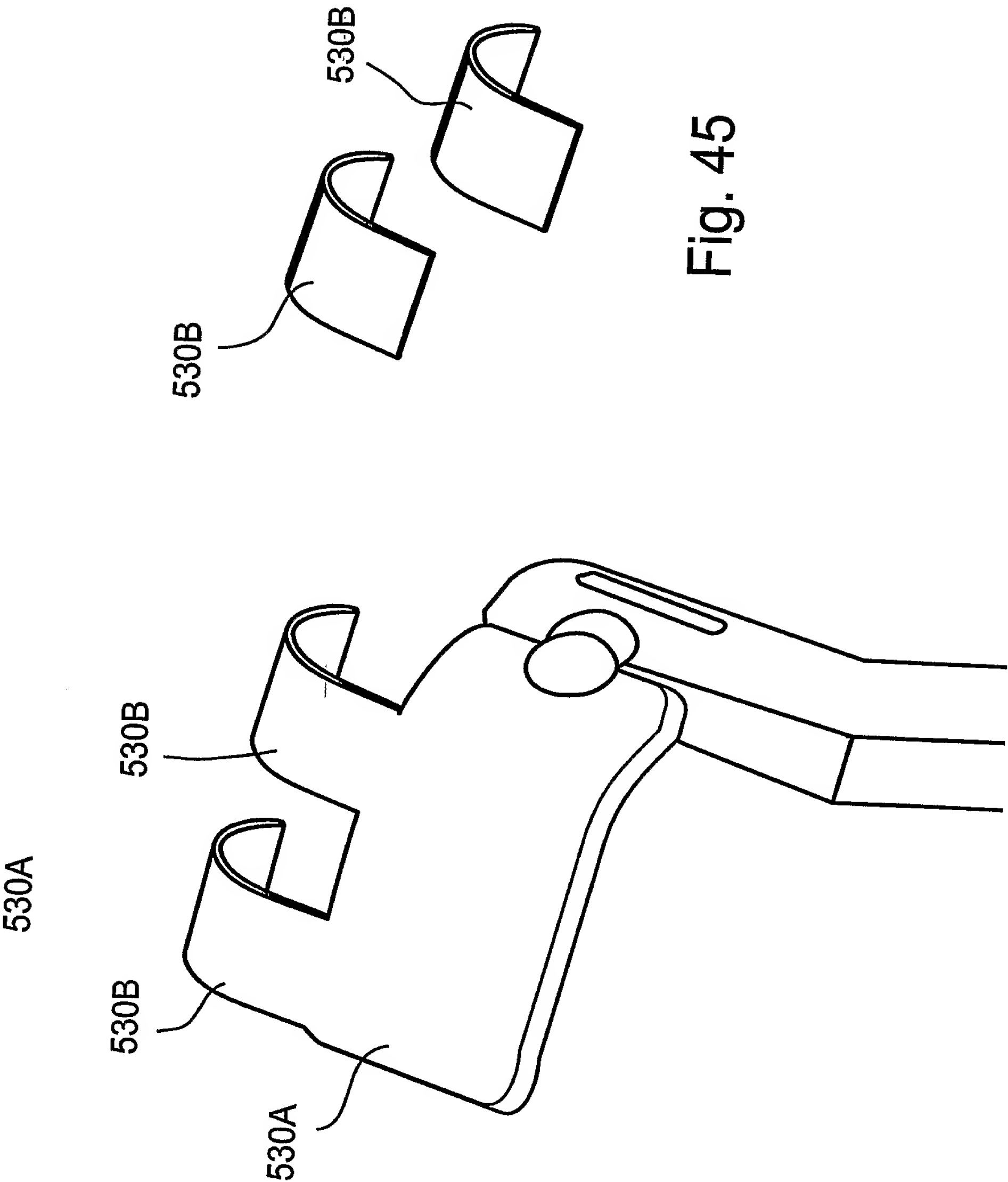


Fig. 45

Fig. 44



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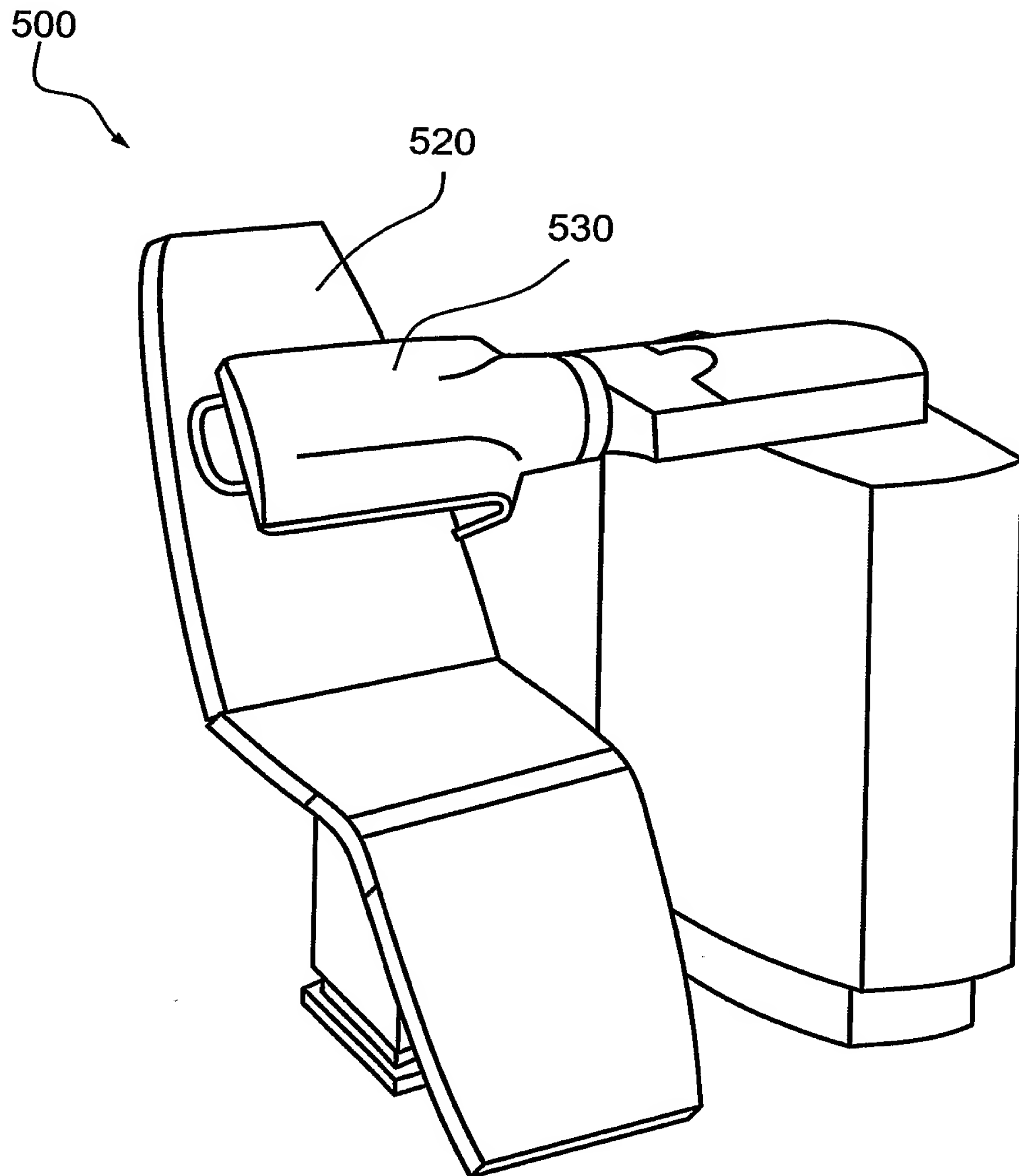


Fig. 46

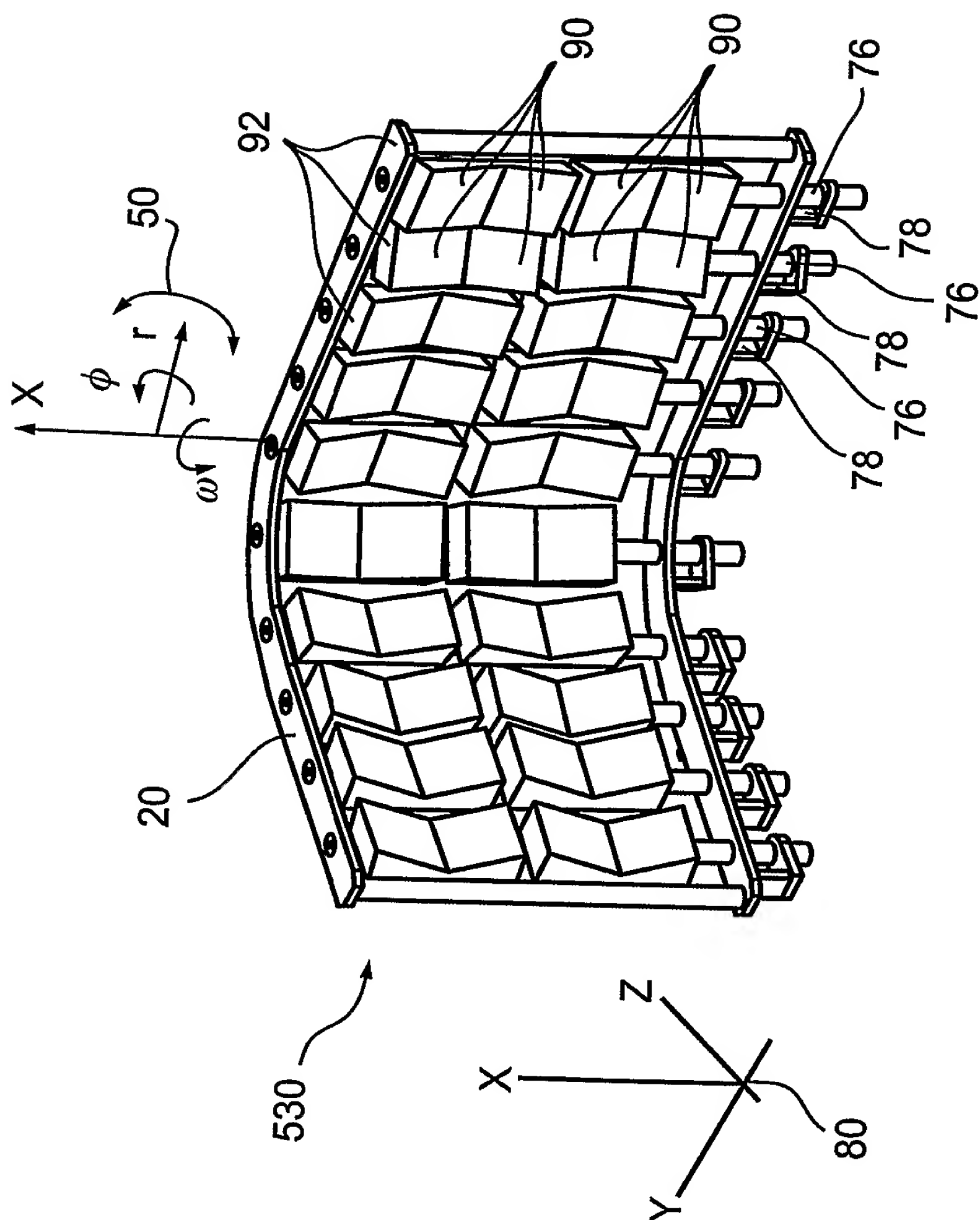


Fig. 47

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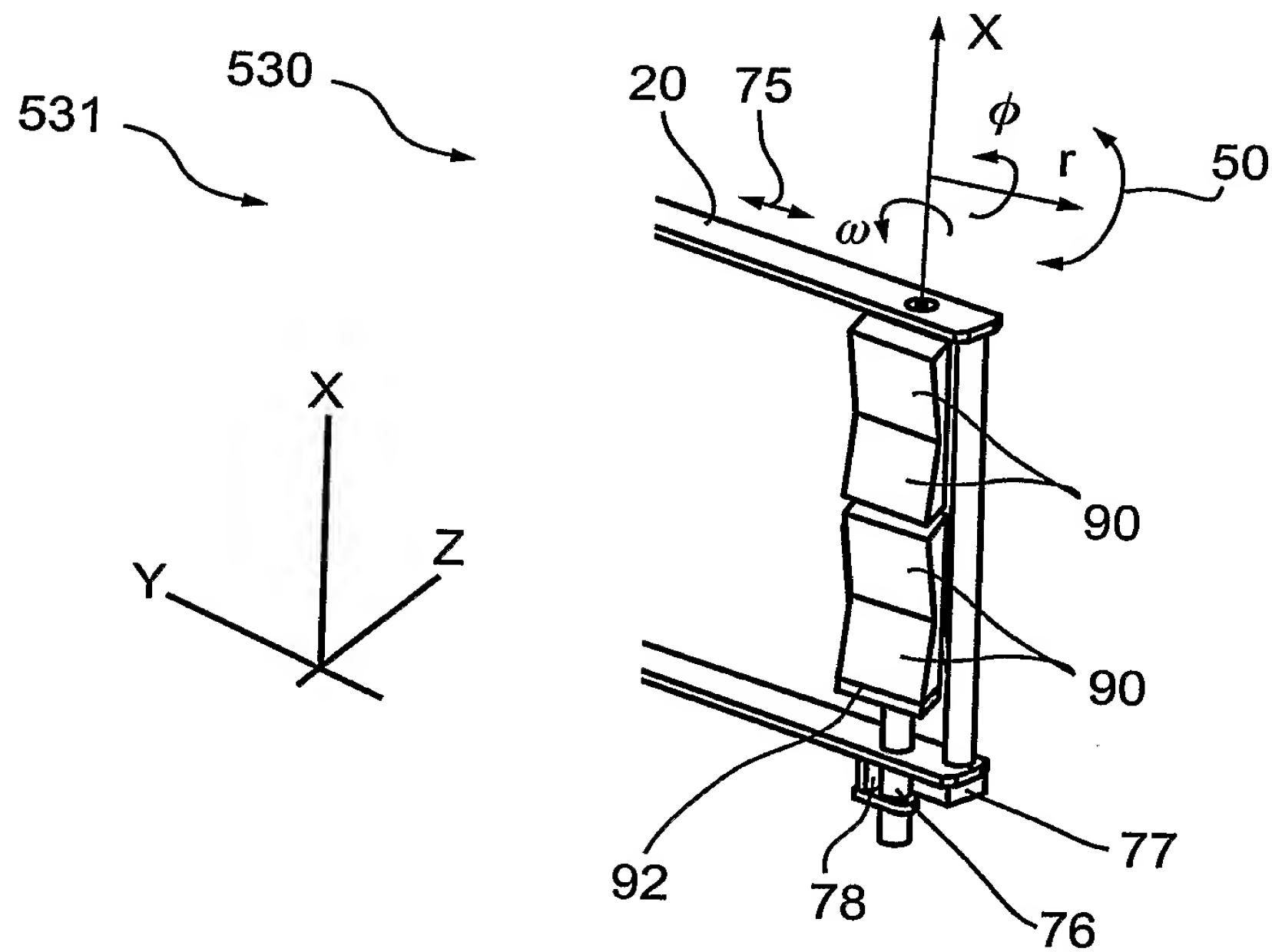
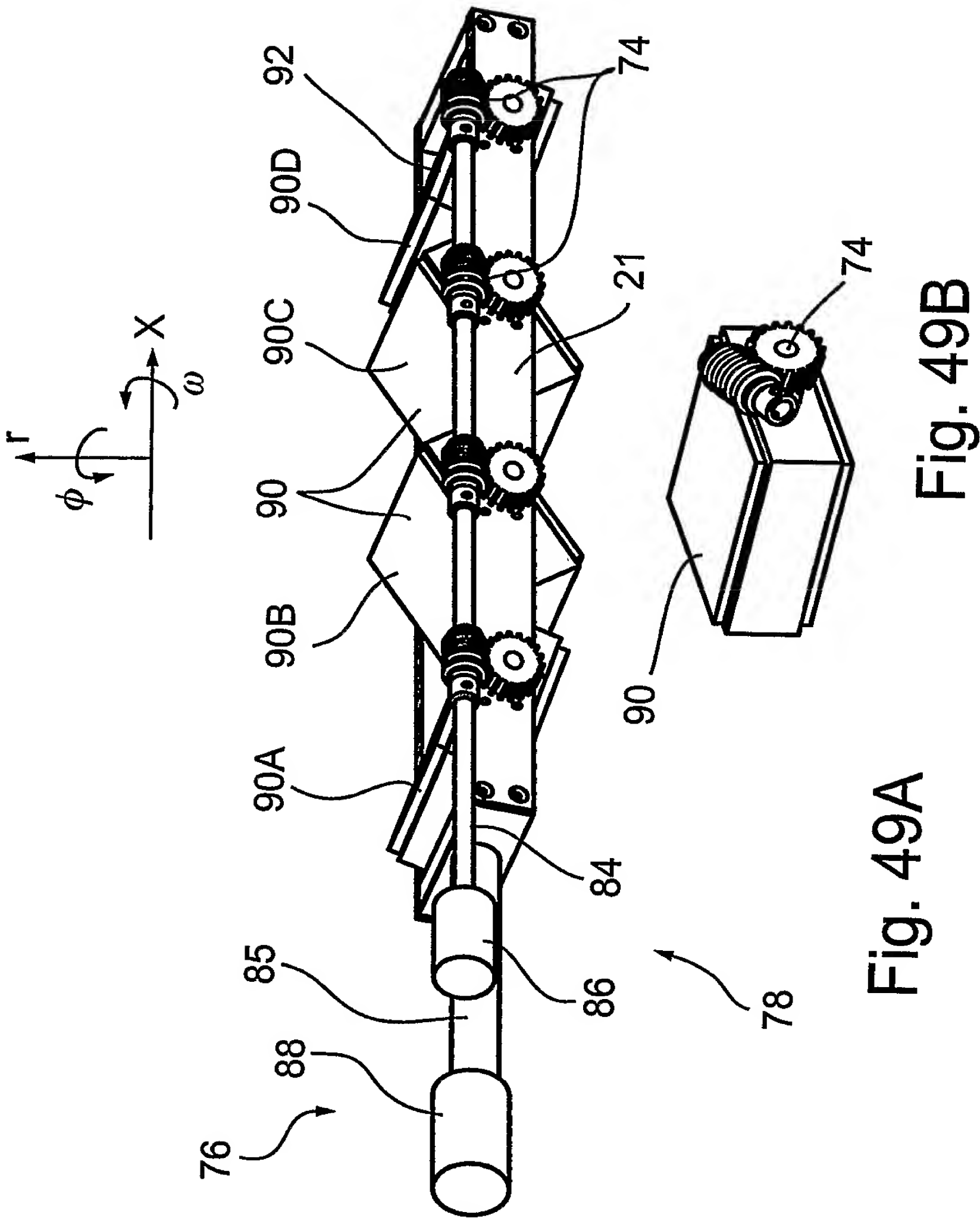


Fig. 48



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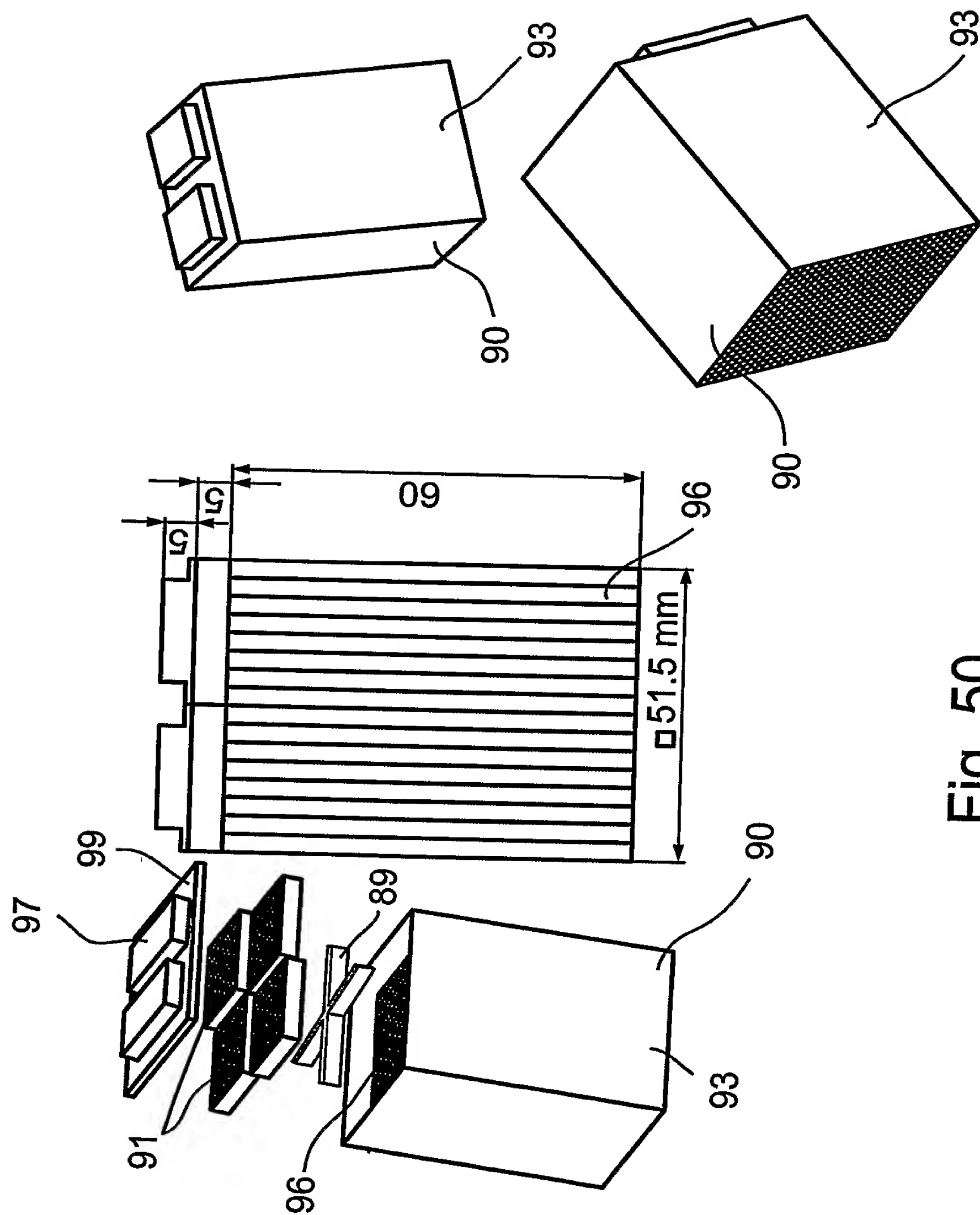


Fig. 50

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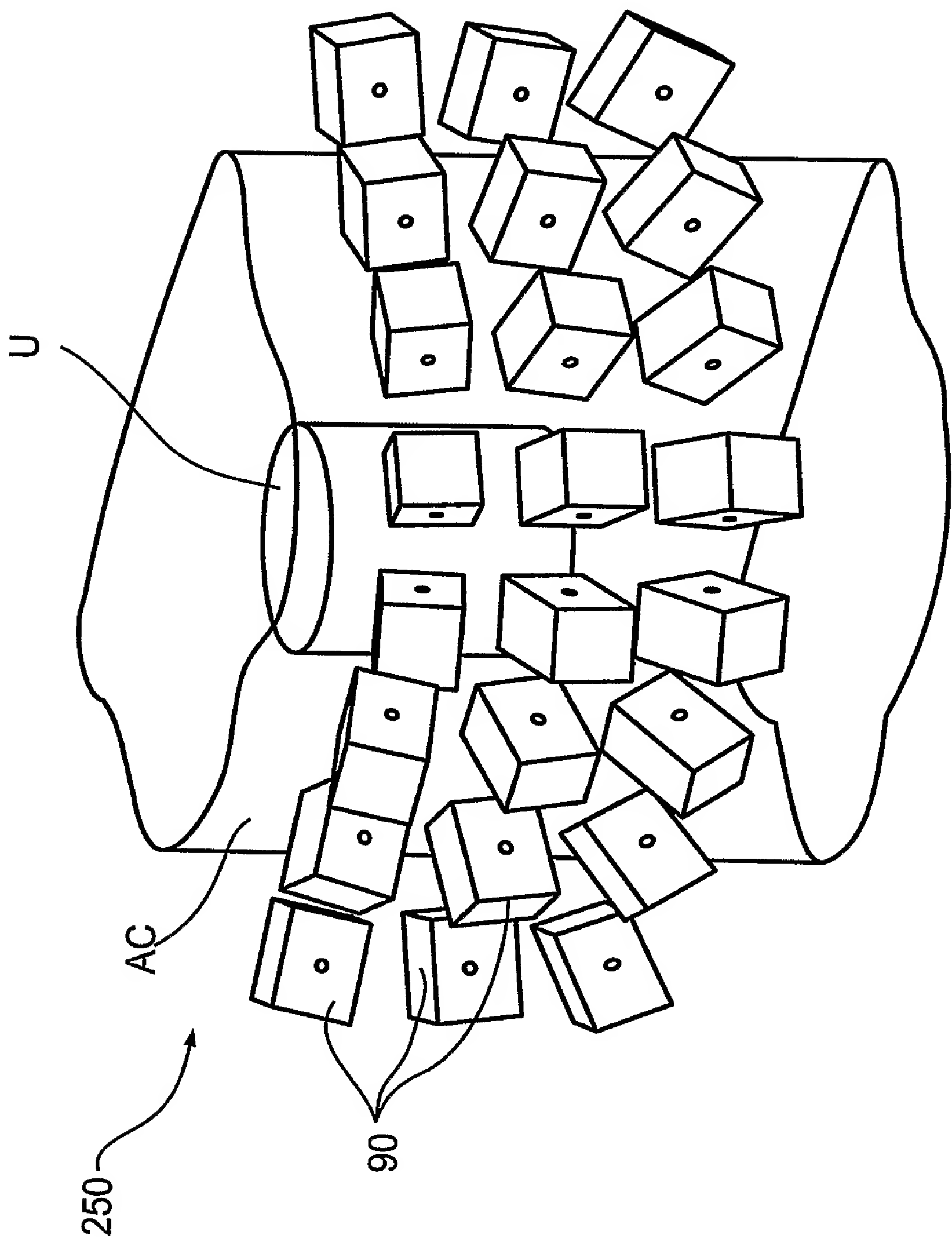
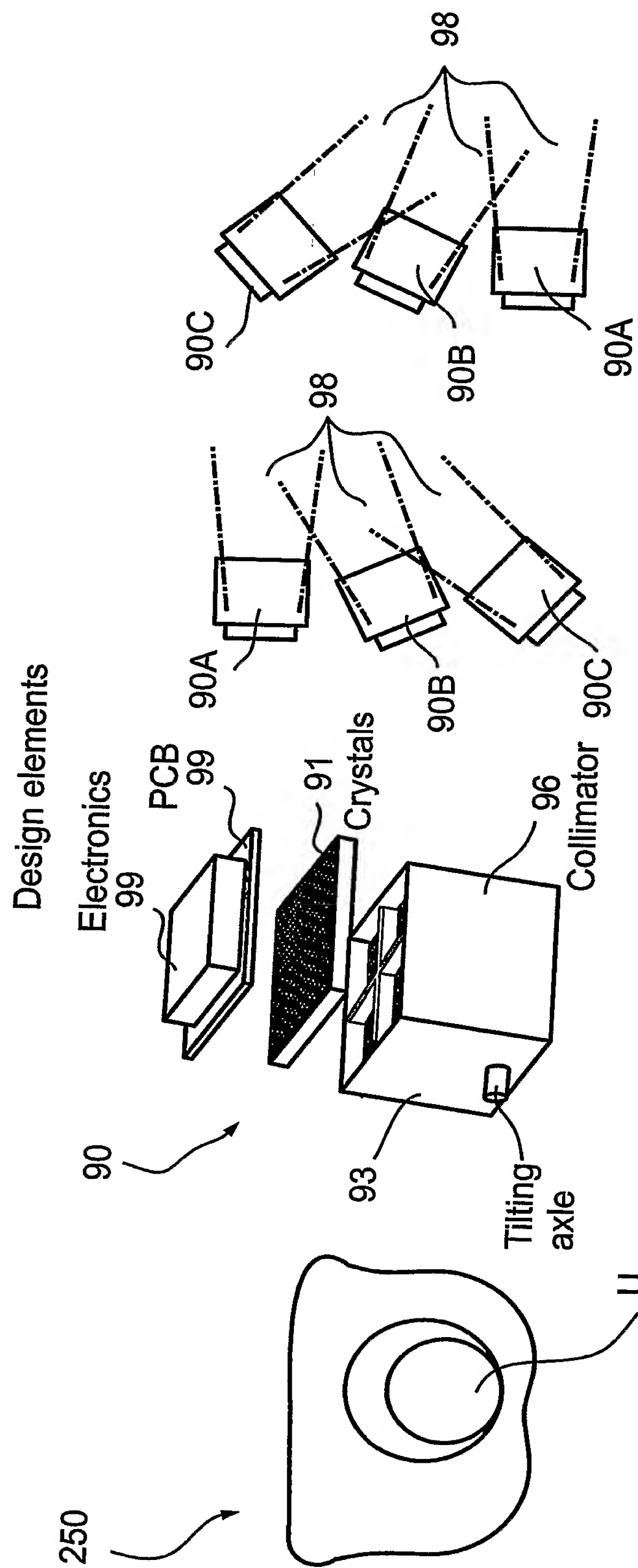


Fig. 51

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**Fig. 52D**

**Fig. 52A**

**Fig. 52C**

**Fig. 52B**

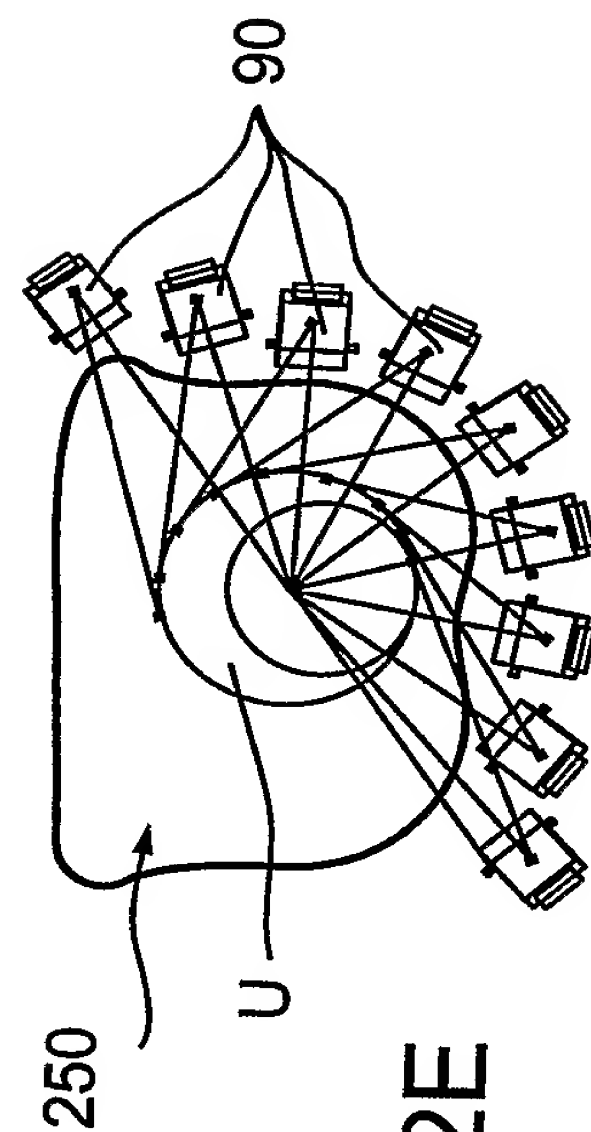


Fig. 52E

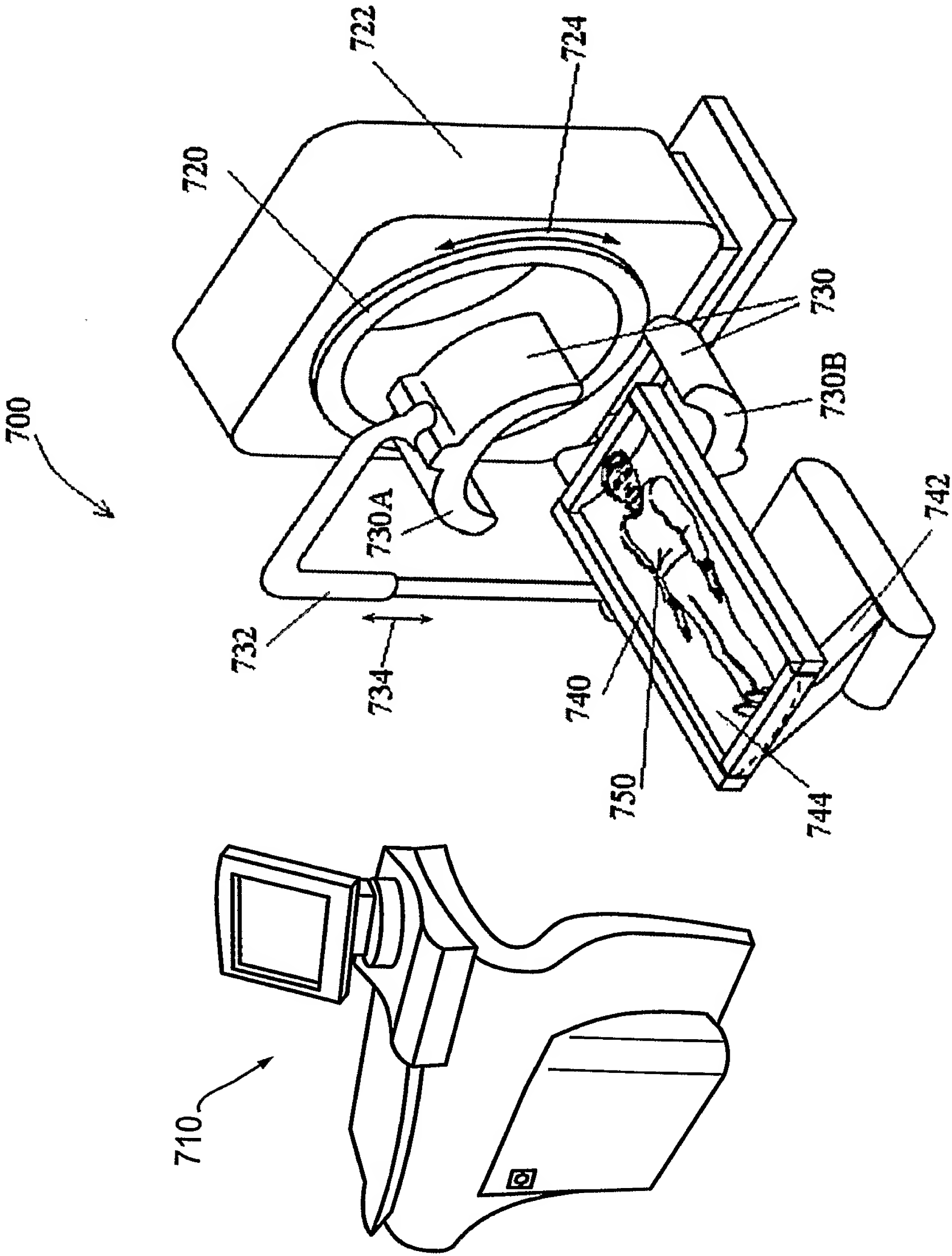


Fig. 53





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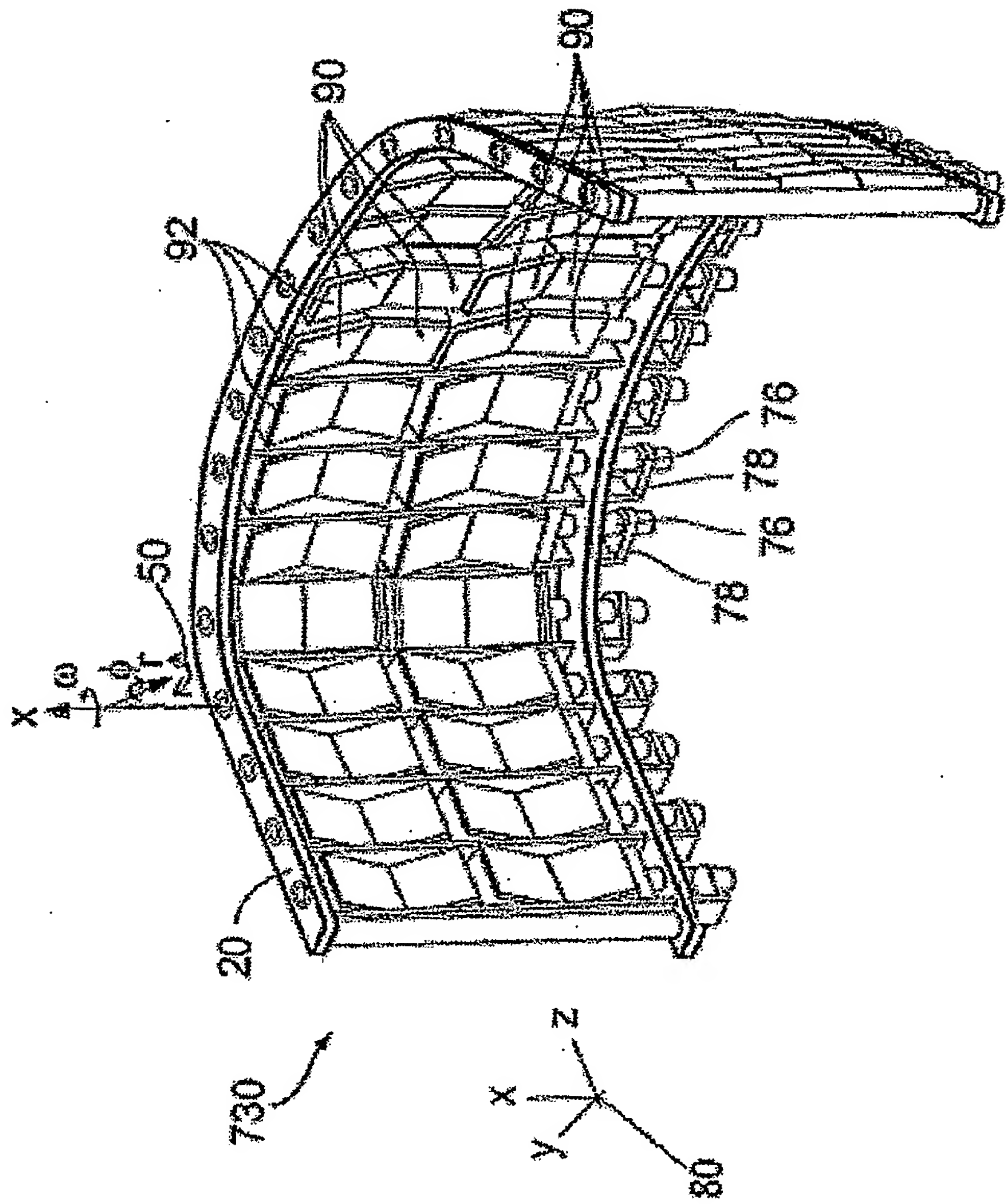


Fig. 55A

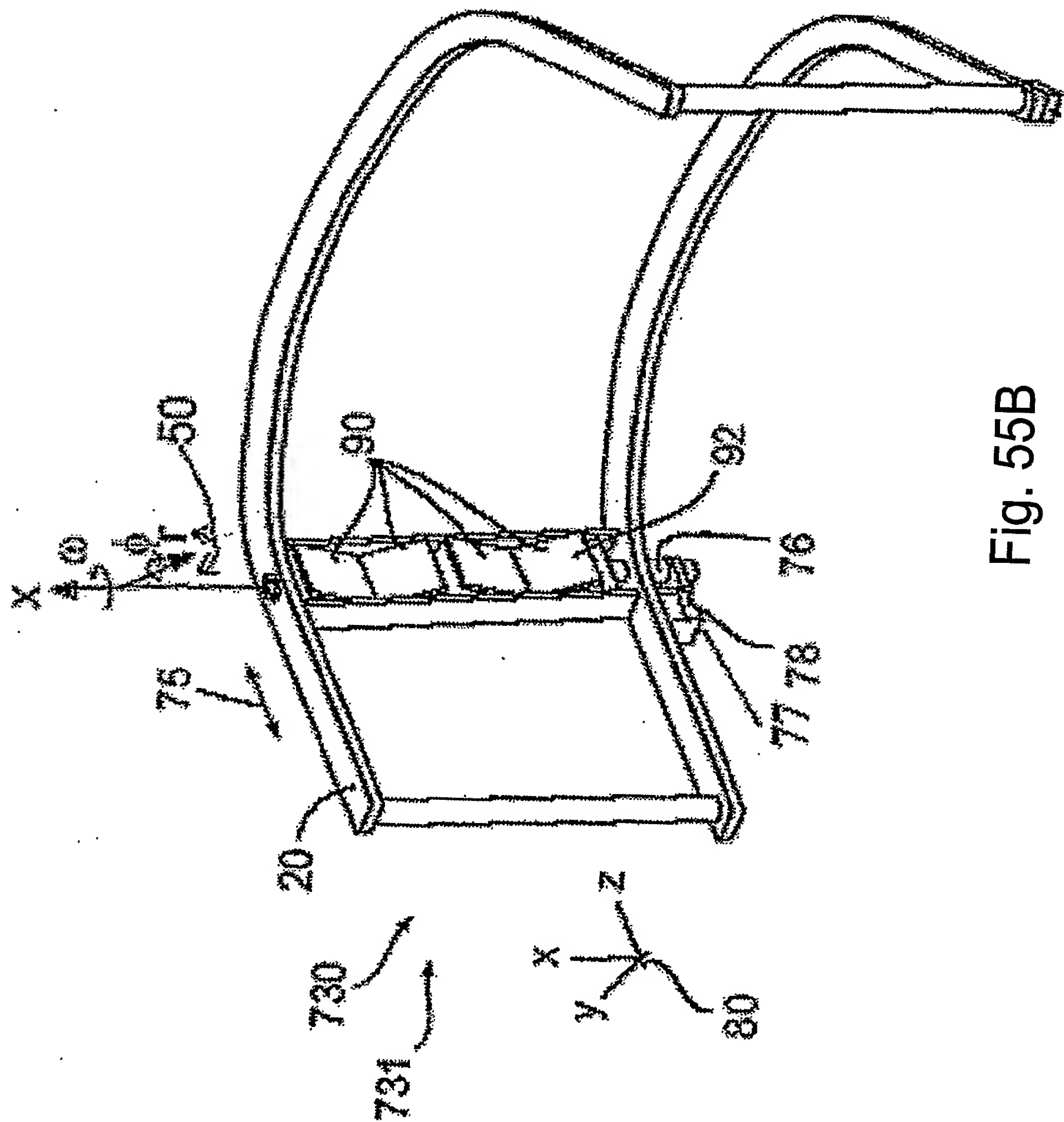


Fig. 55B

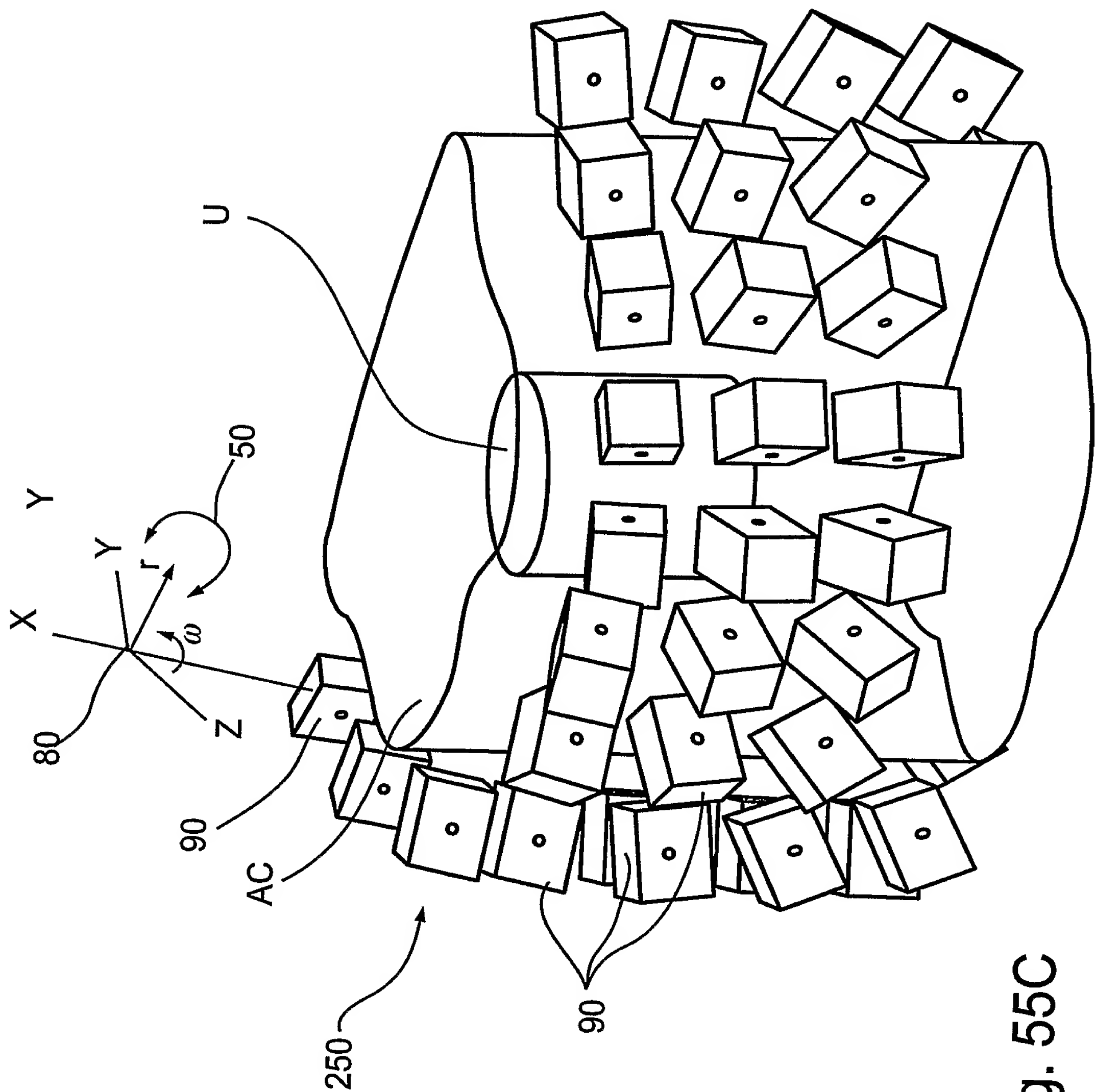
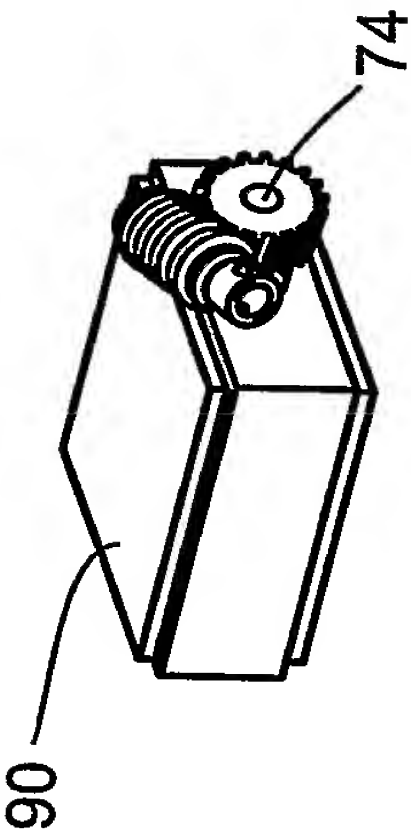
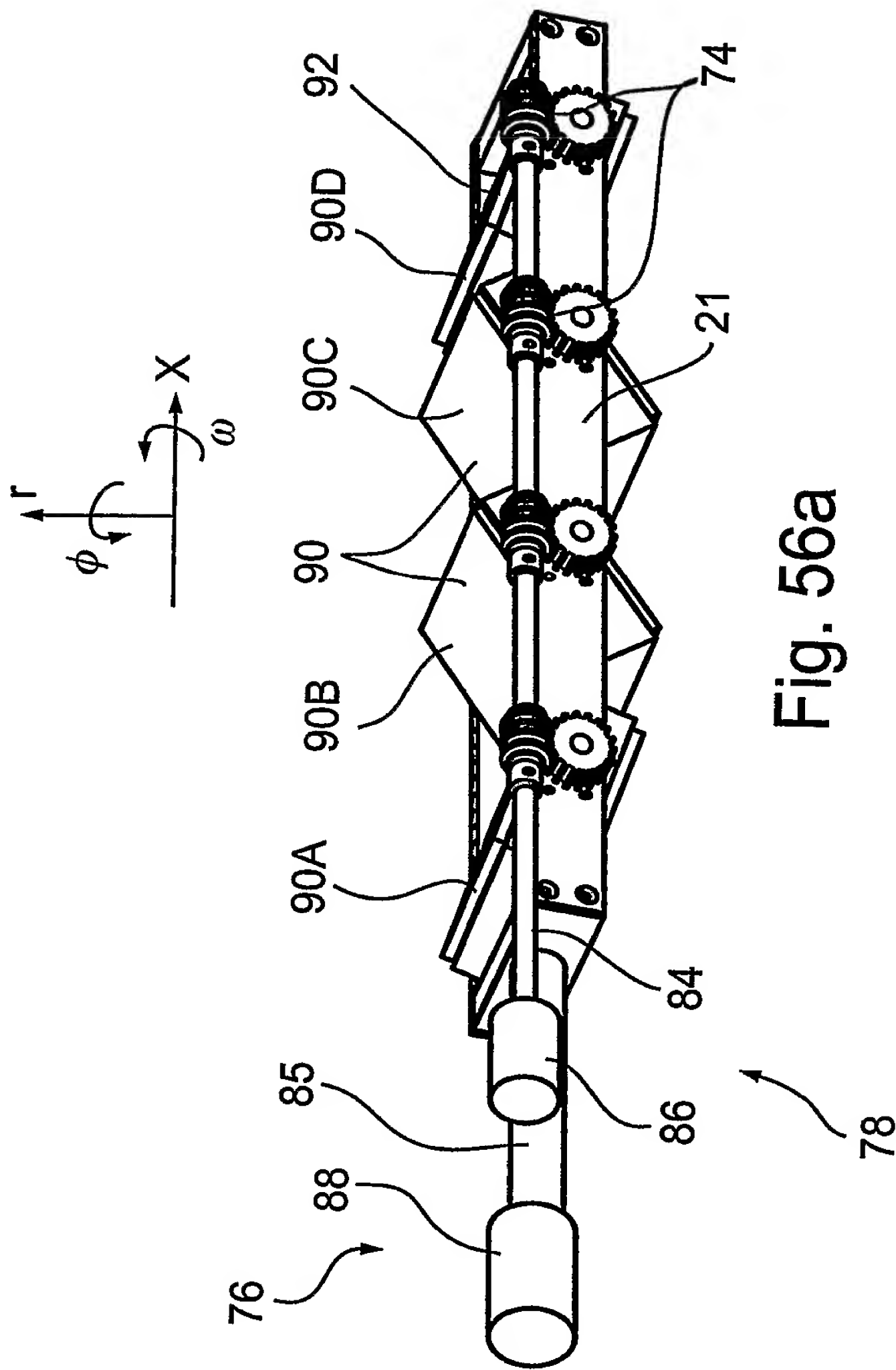


Fig. 55C



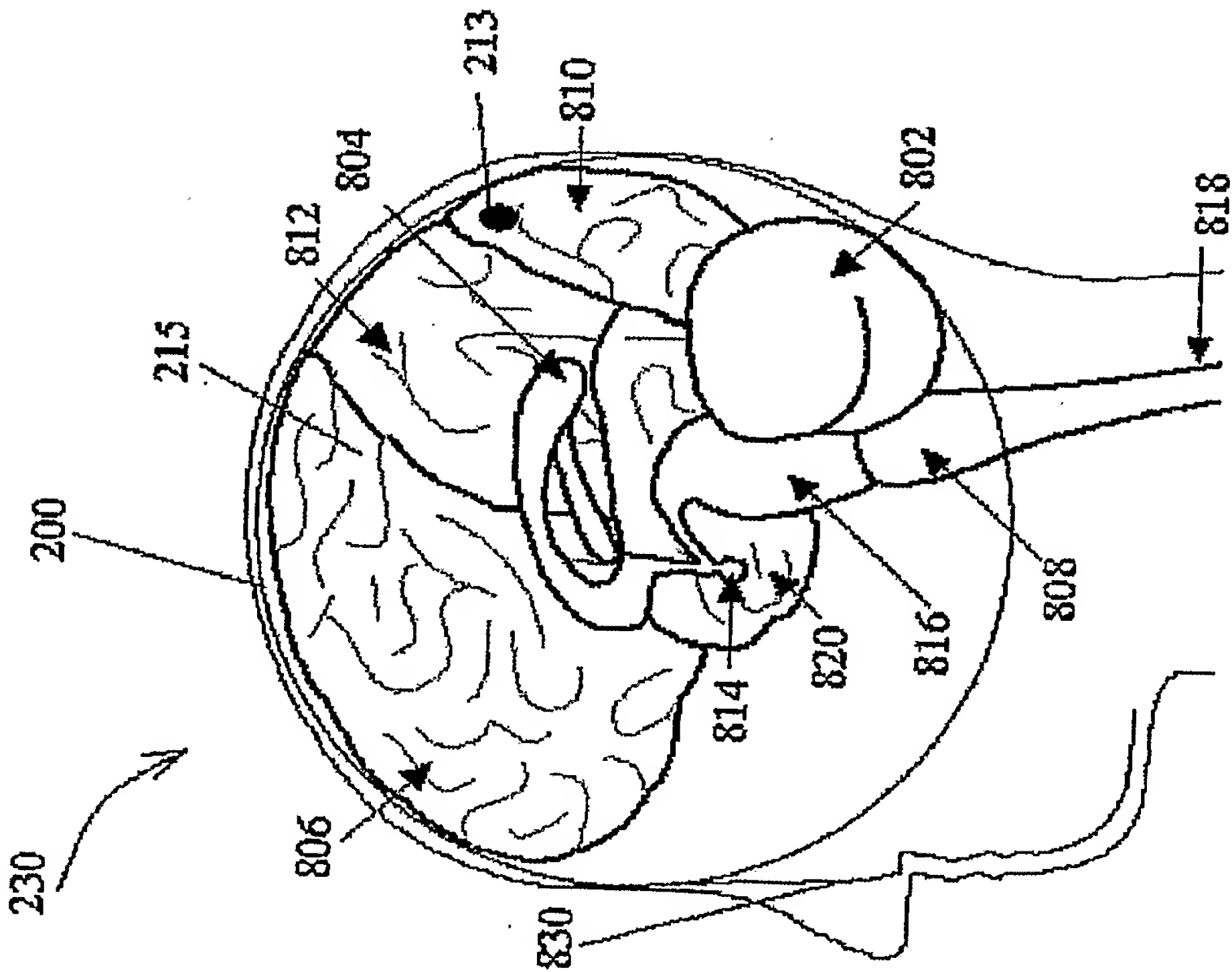


Fig. 57A

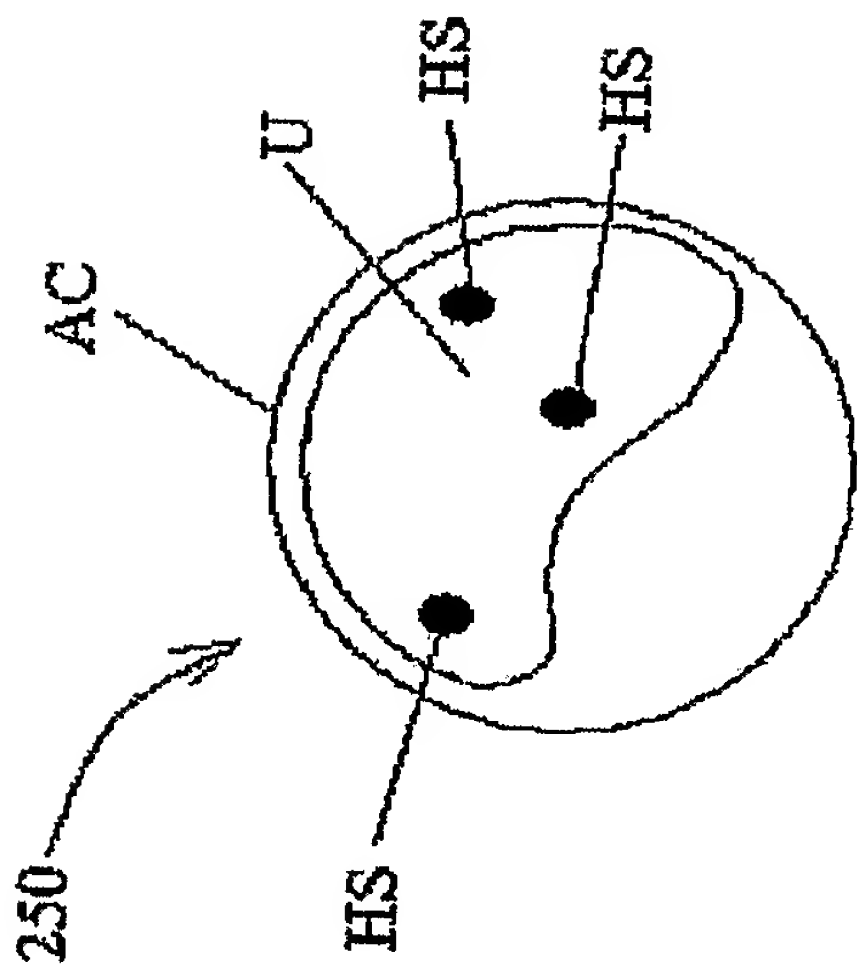


Fig. 57B

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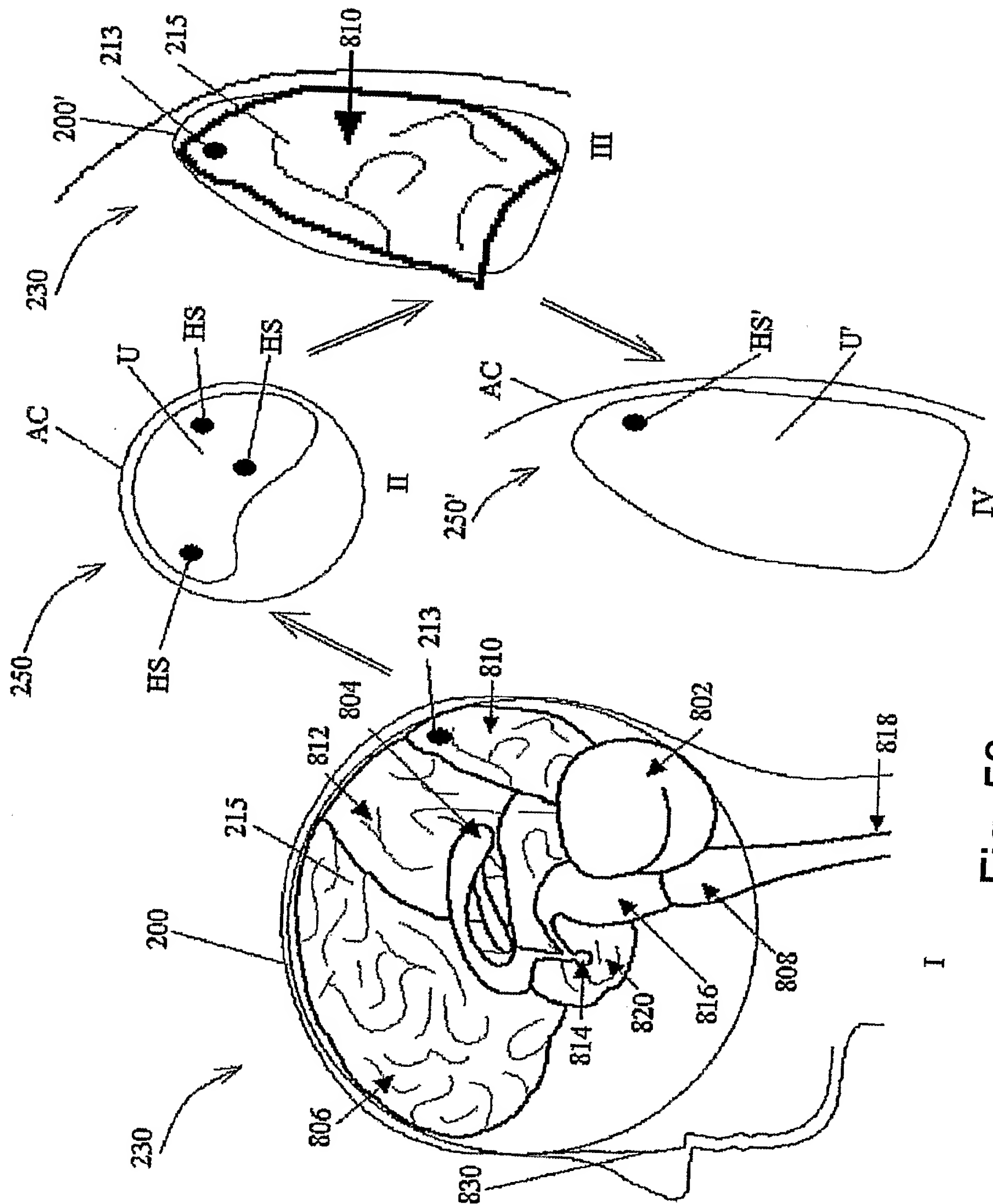
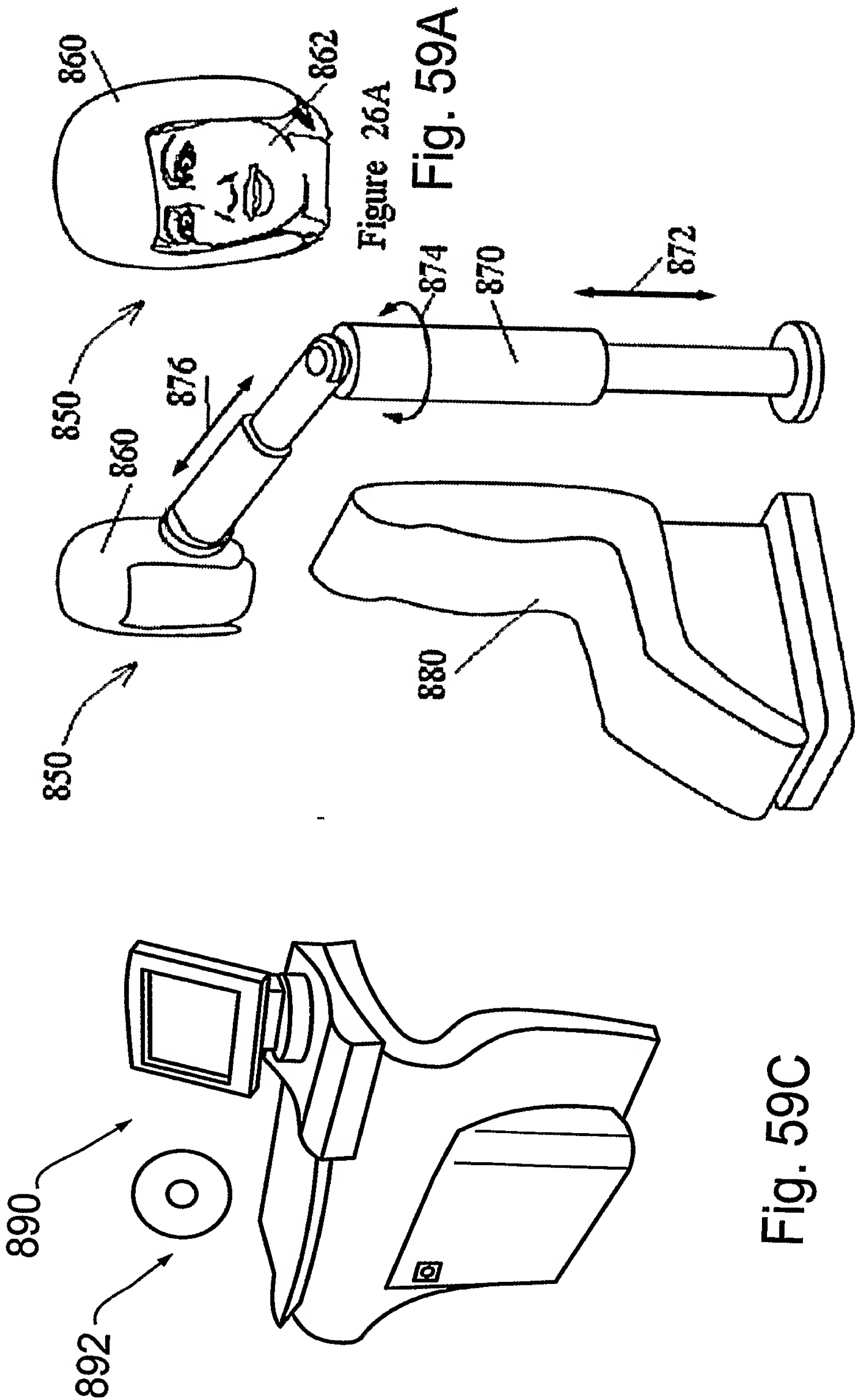


Fig. 58





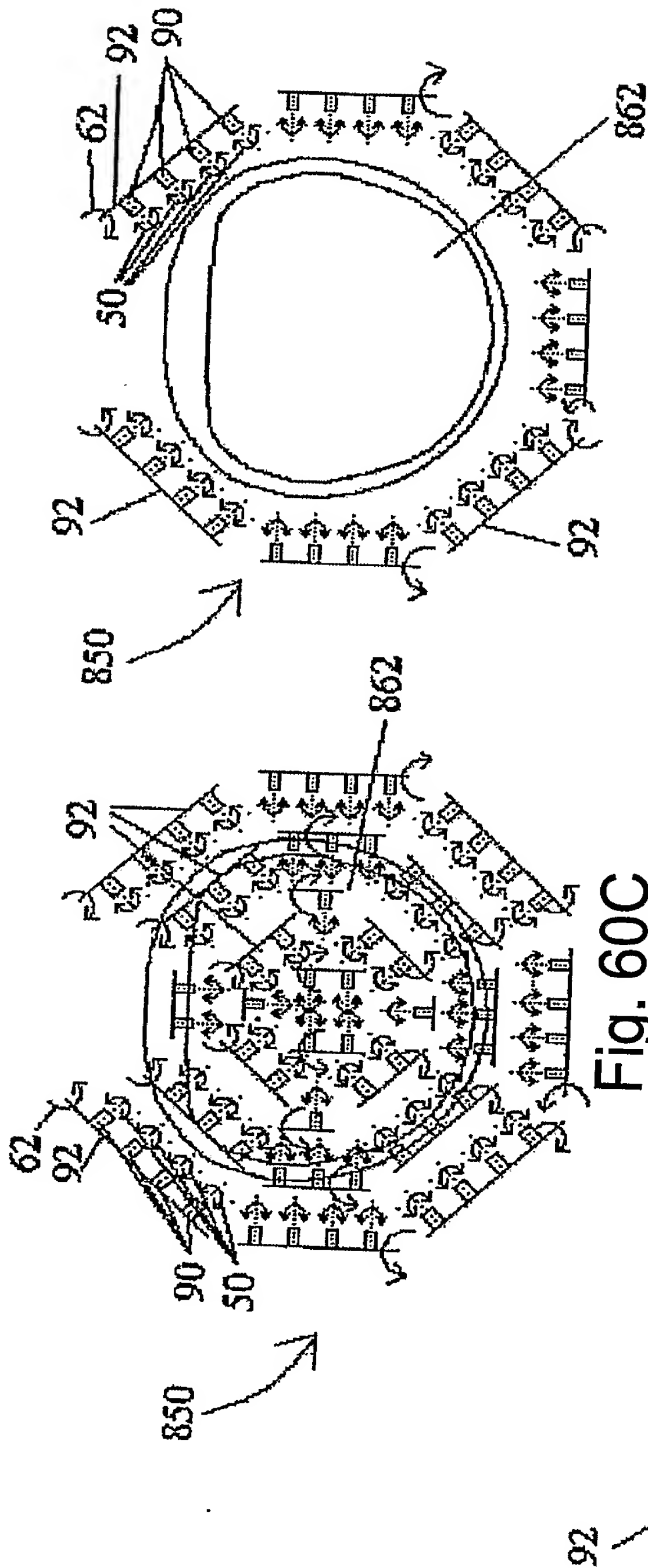


Fig. 60B

Fig. 60A

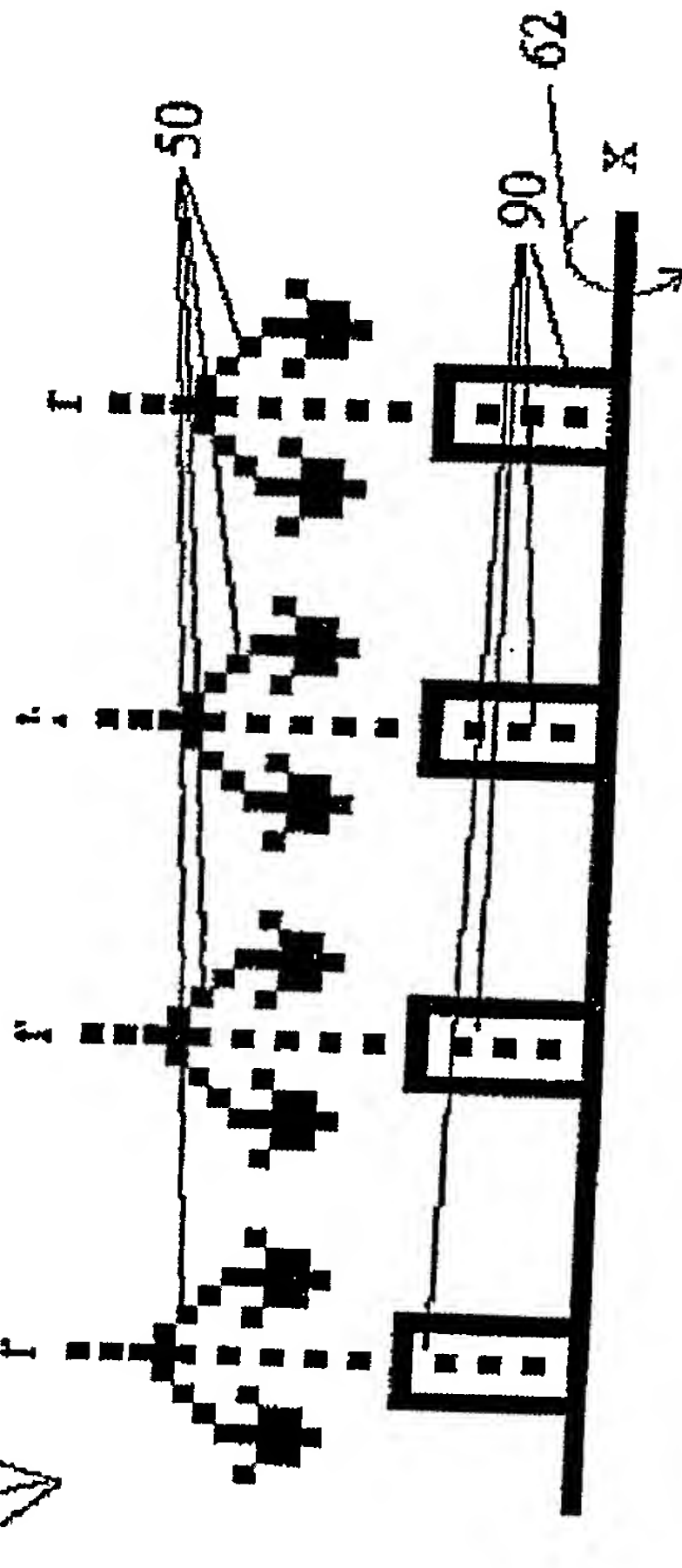


Fig. 60C

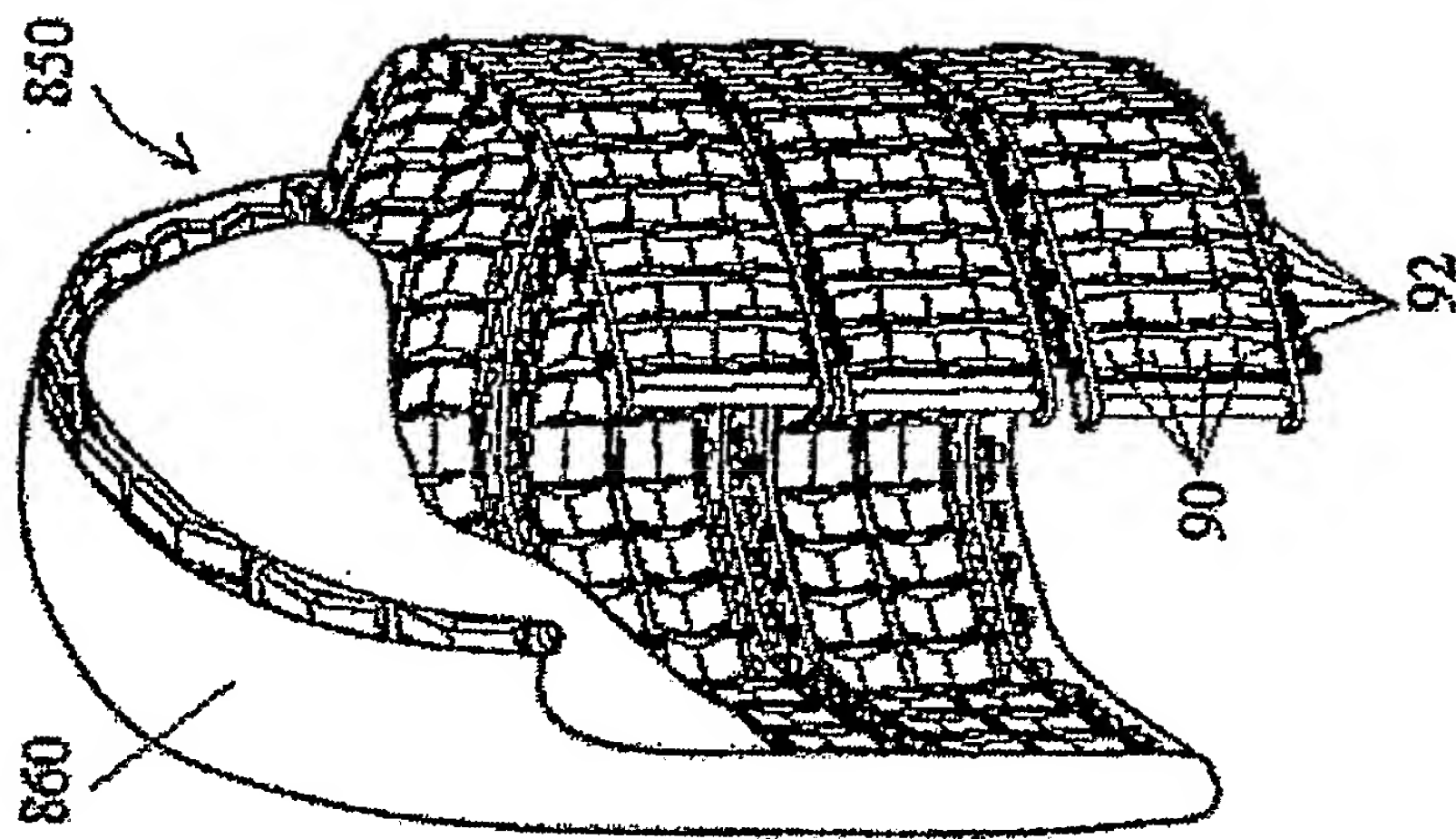


Fig. 60F

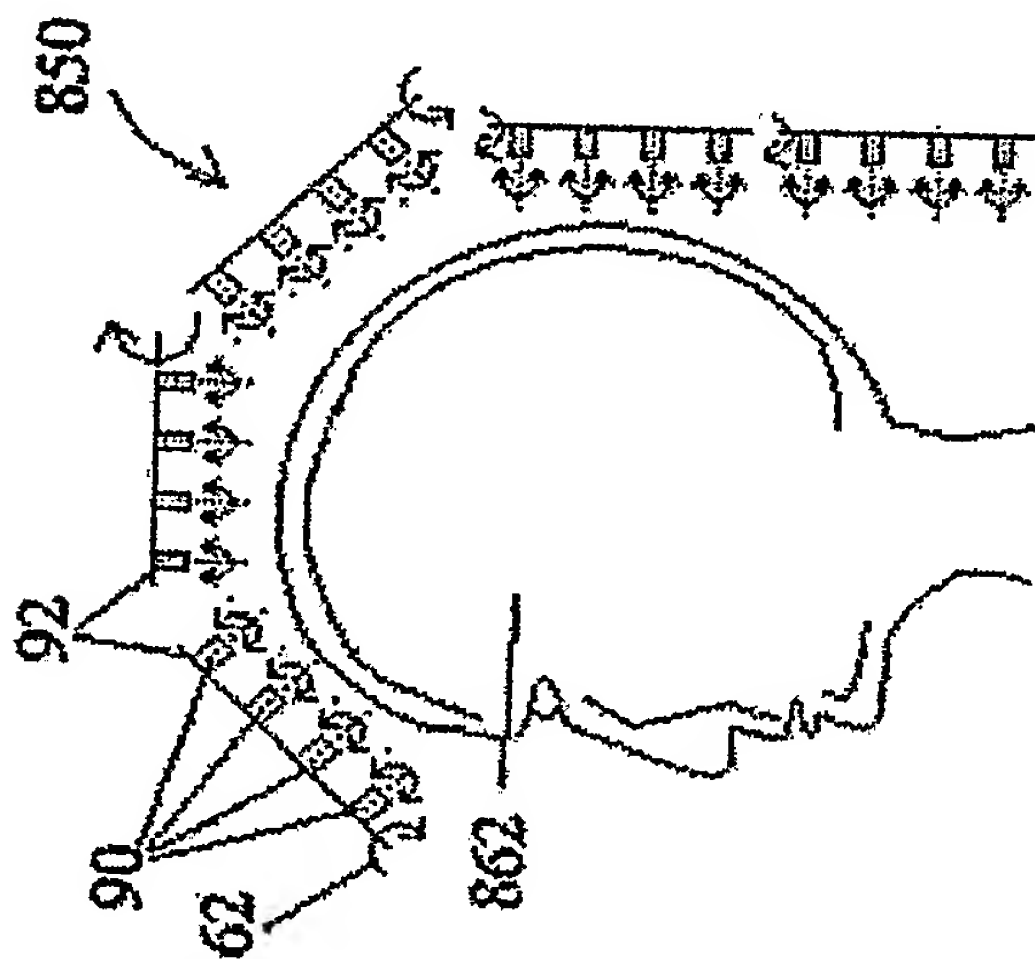


Fig. 60E

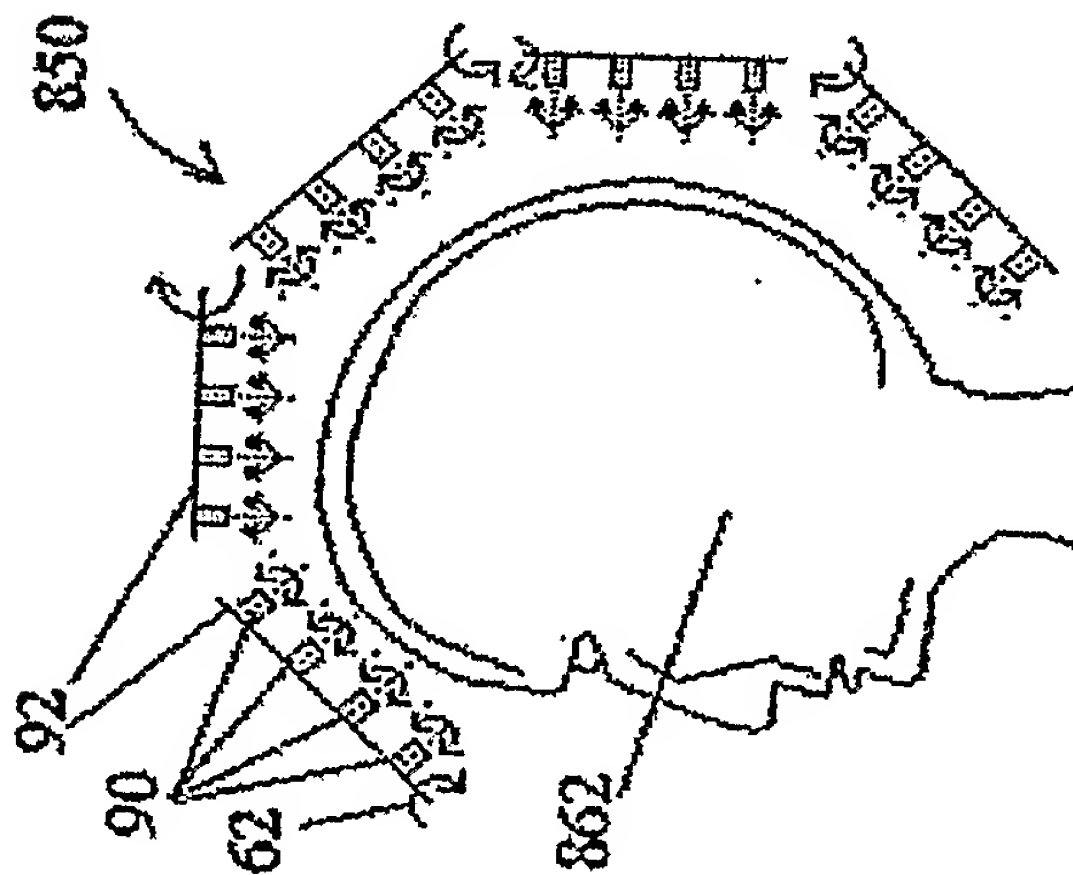
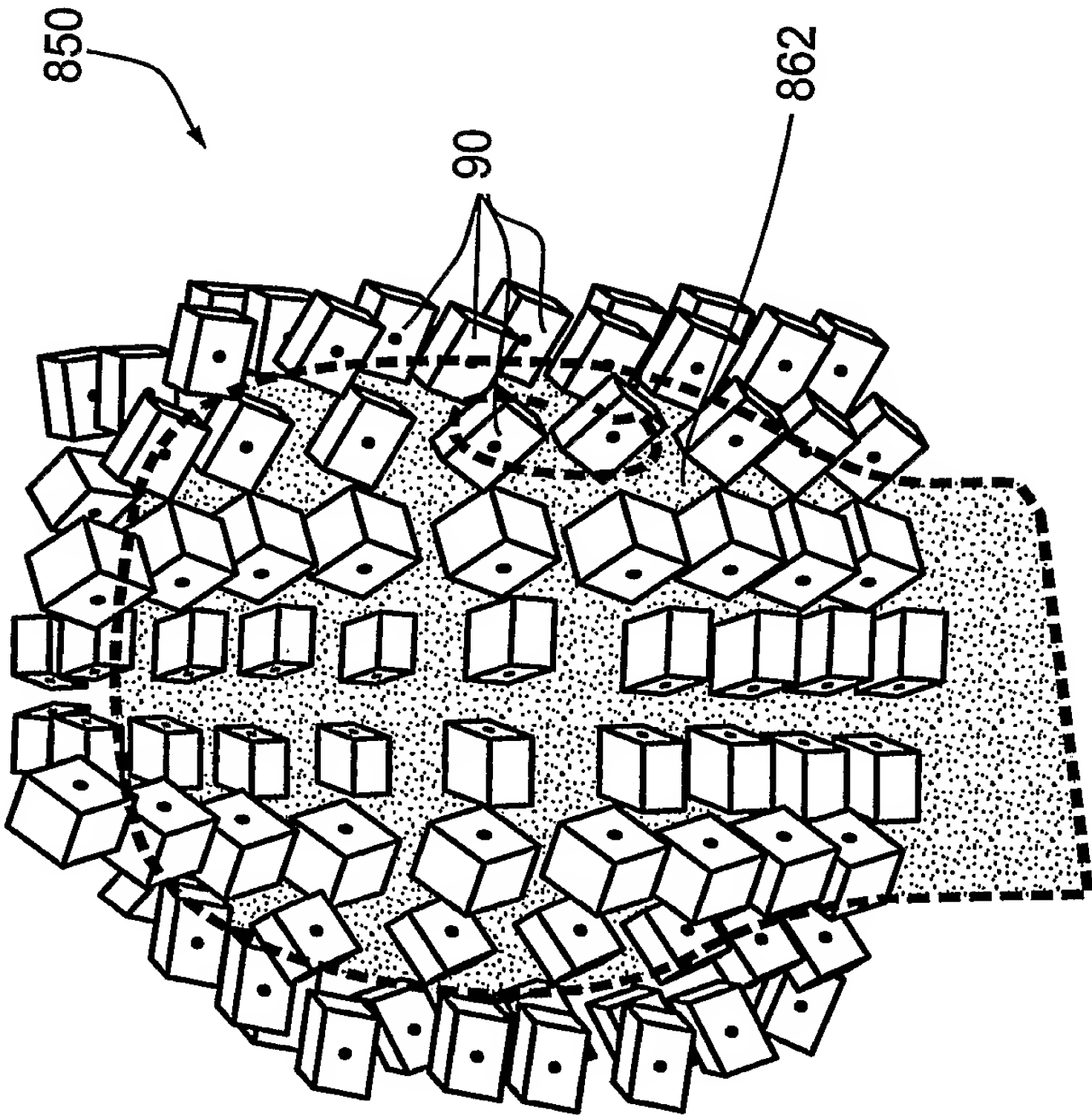
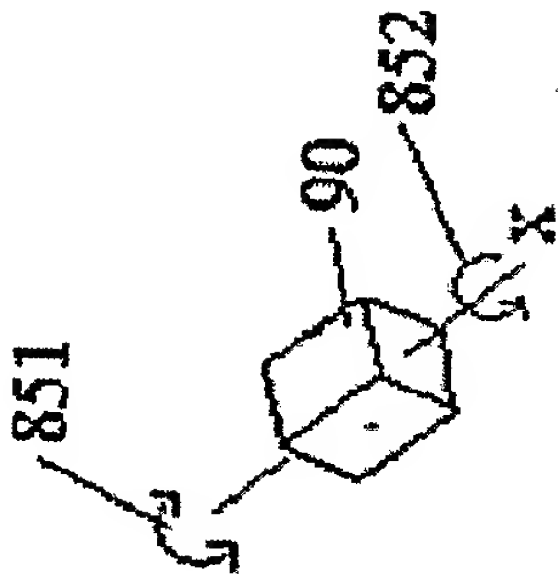
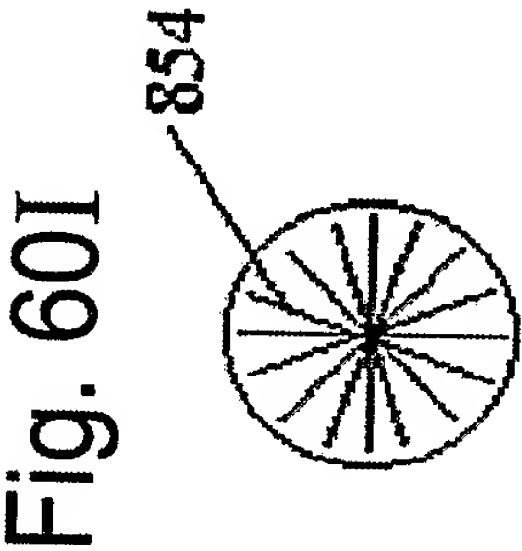
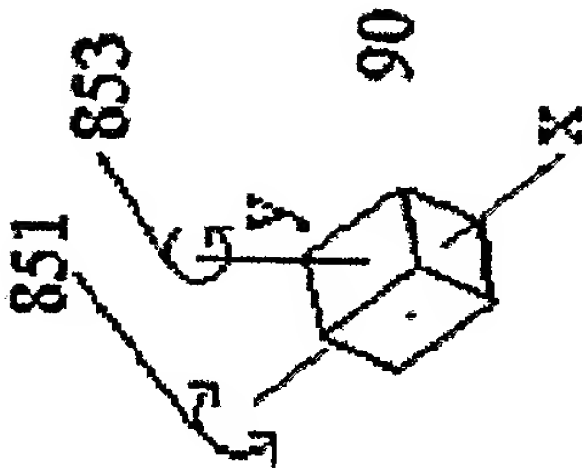
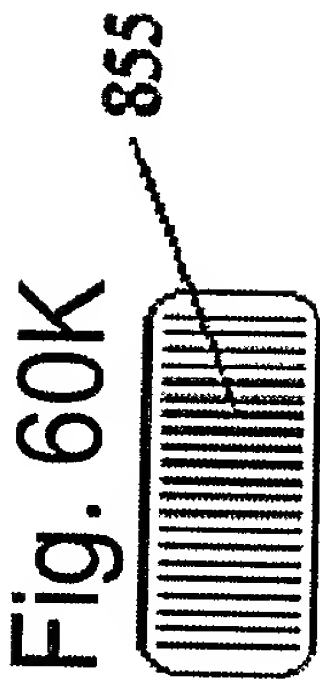


Fig. 60D



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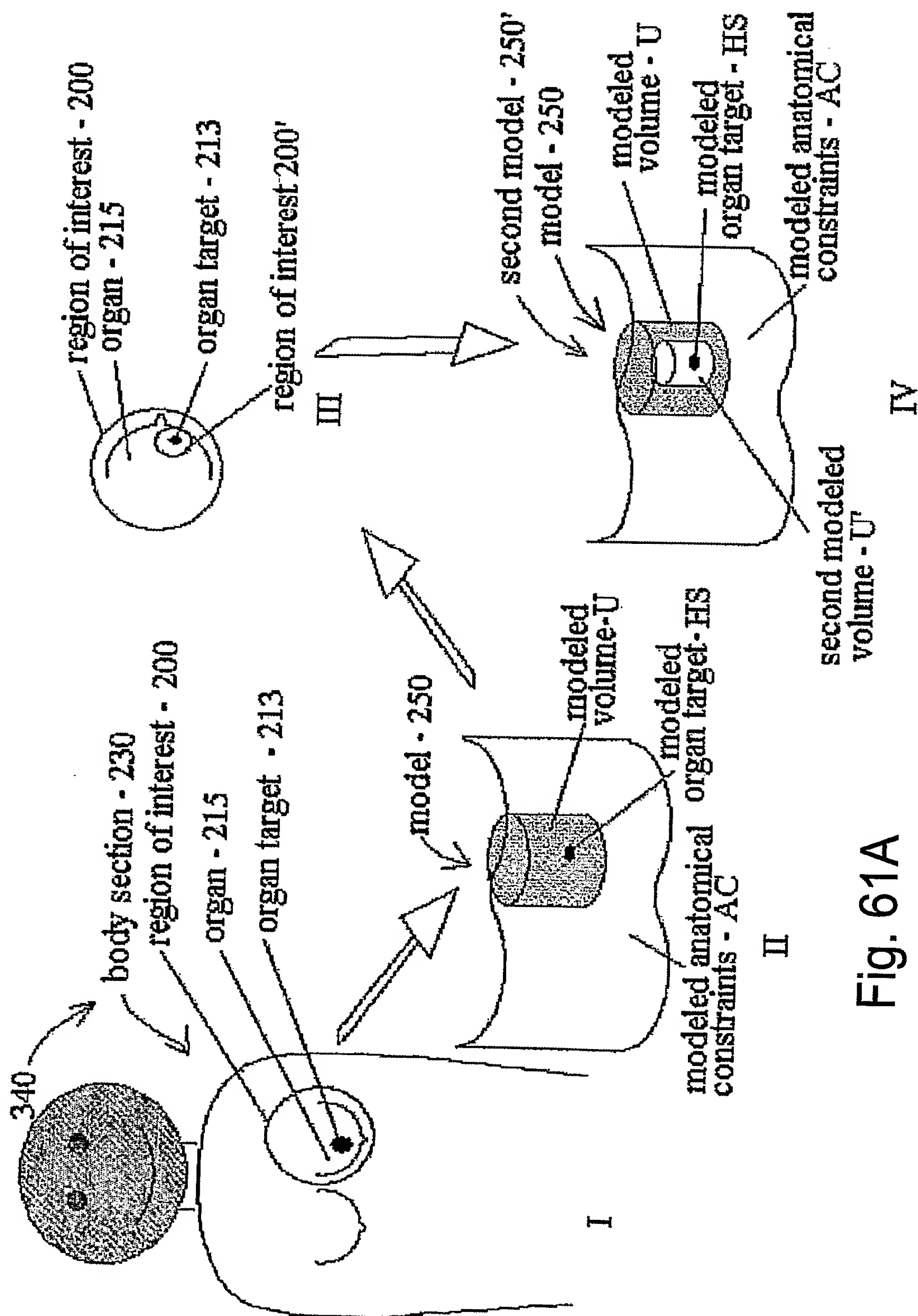


Fig. 61A

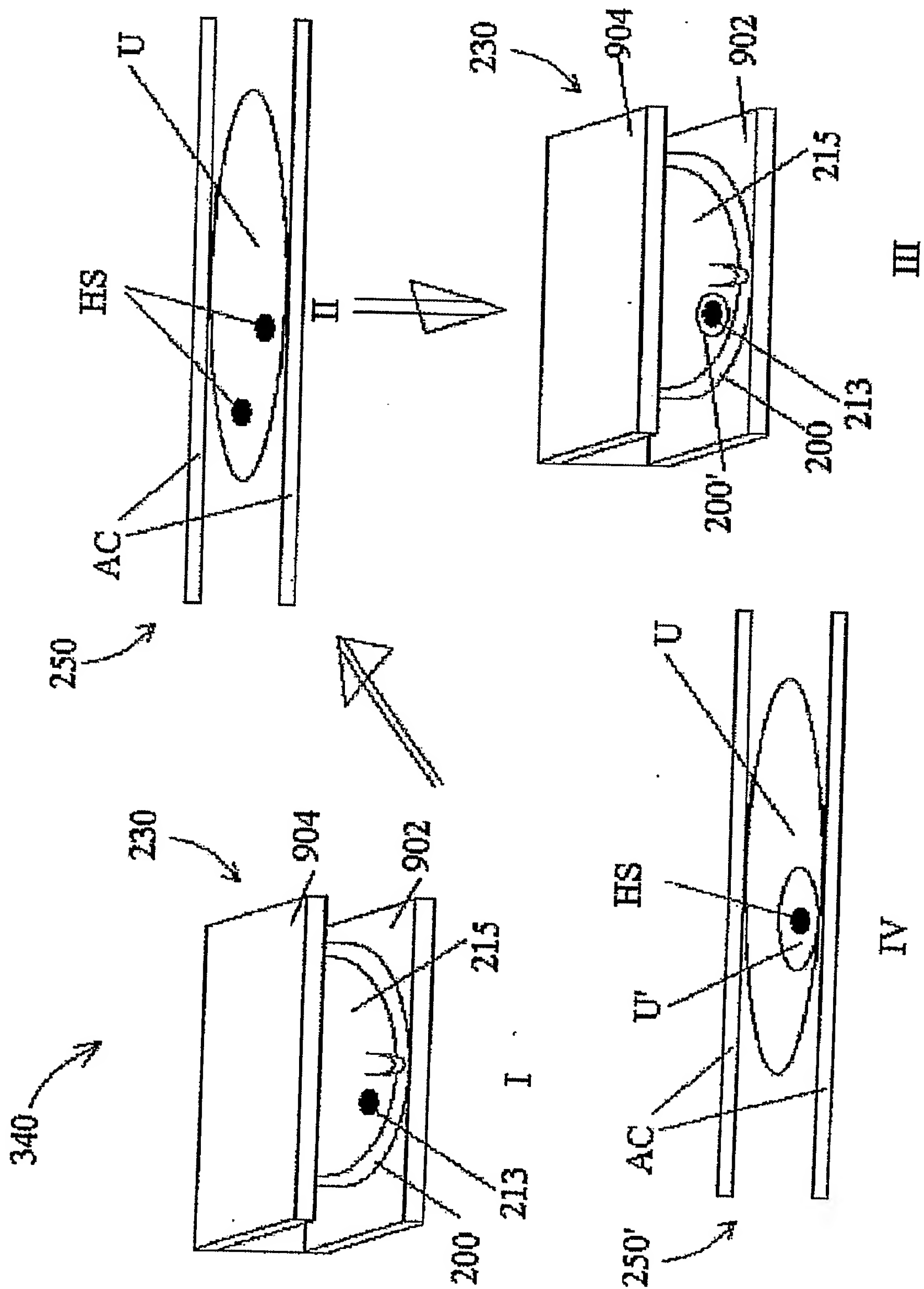


Fig. 61B

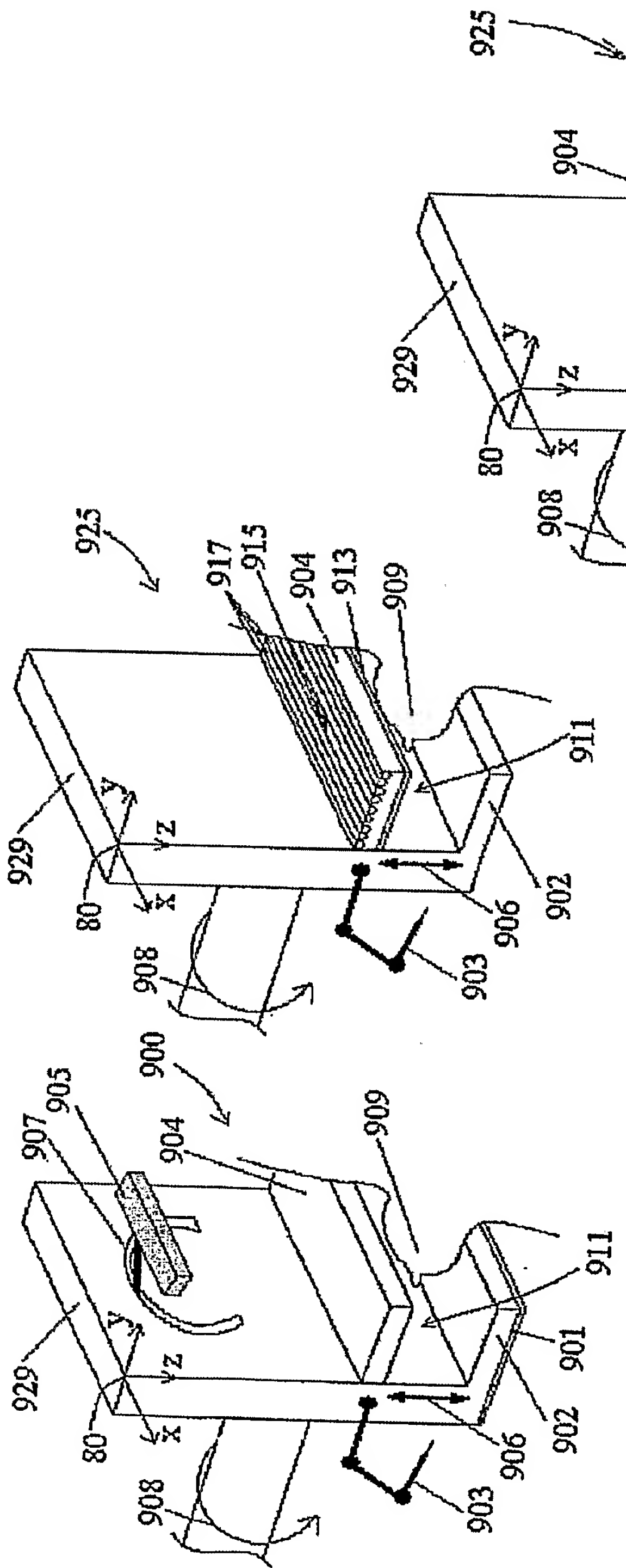
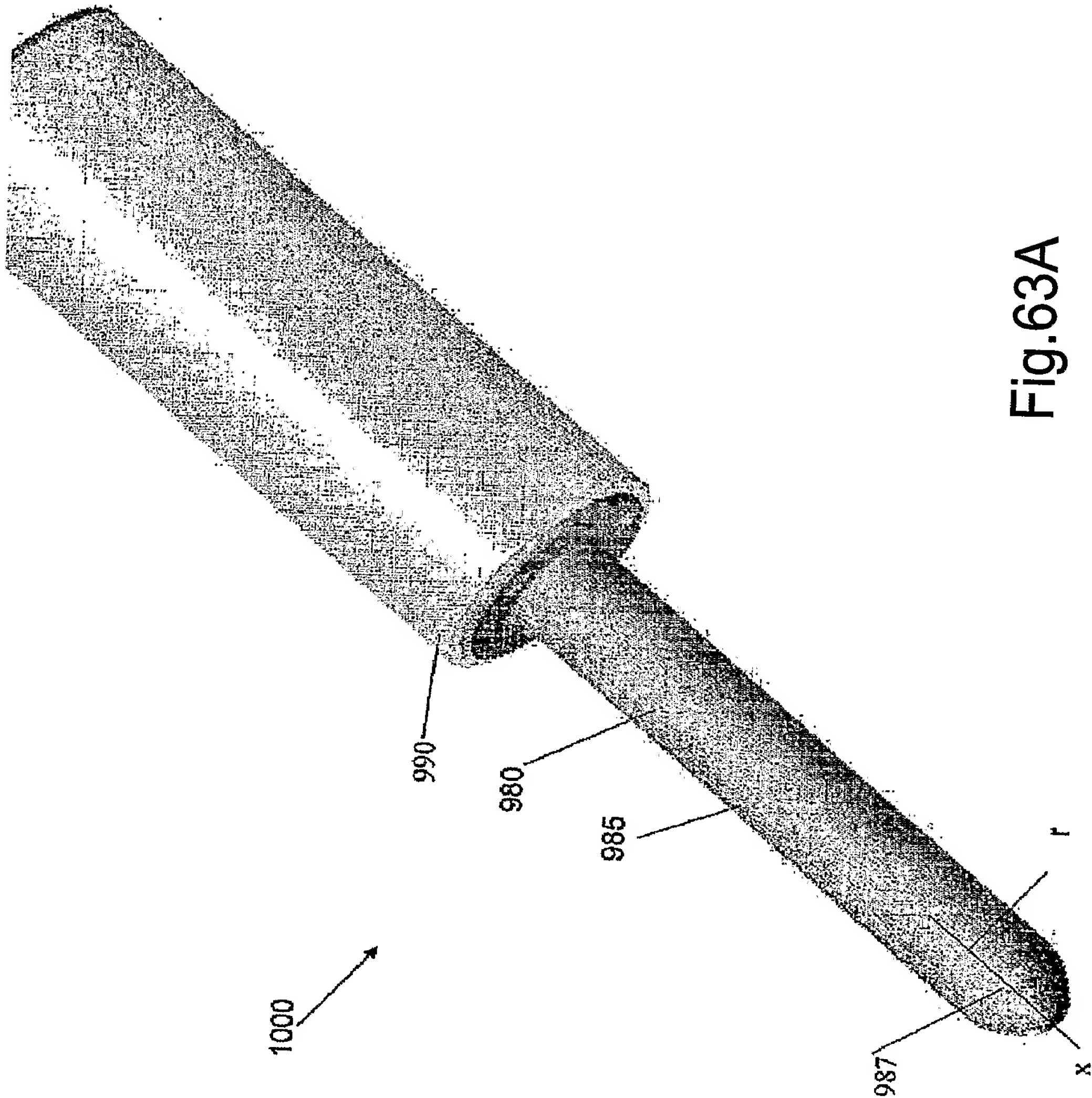


Fig. 62A

Fig. 62B

Fig. 62C



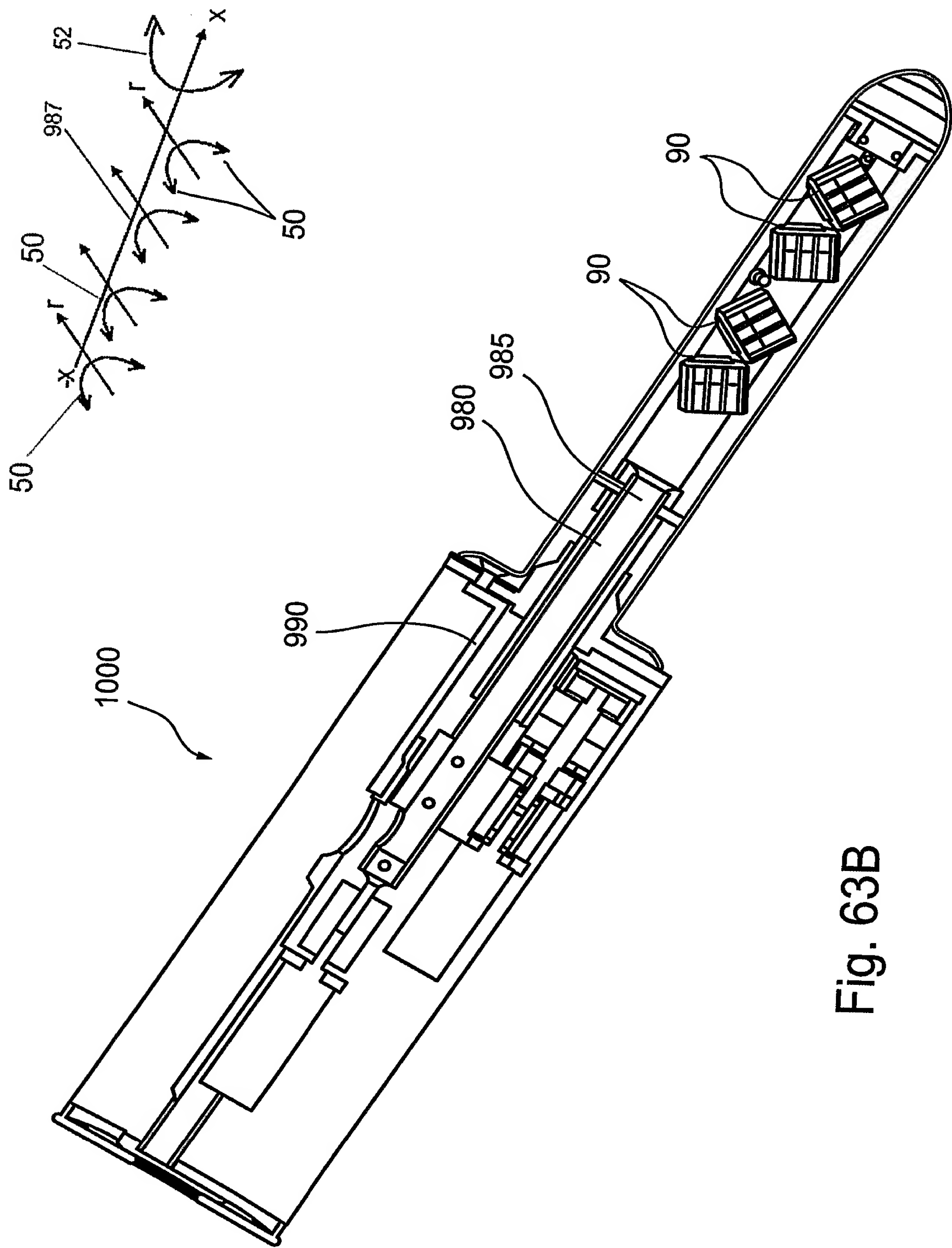


Fig. 63B



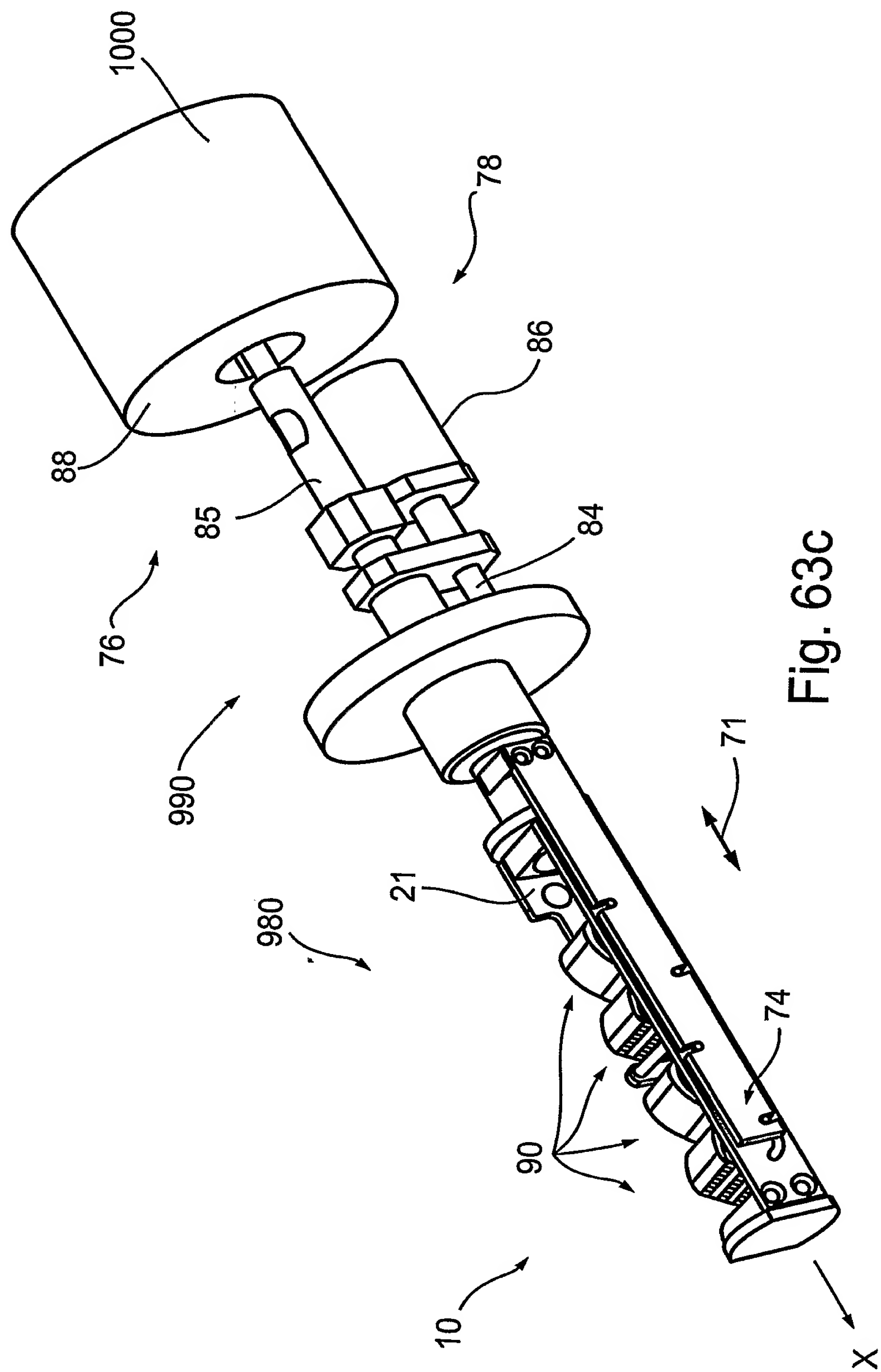


Fig. 63C

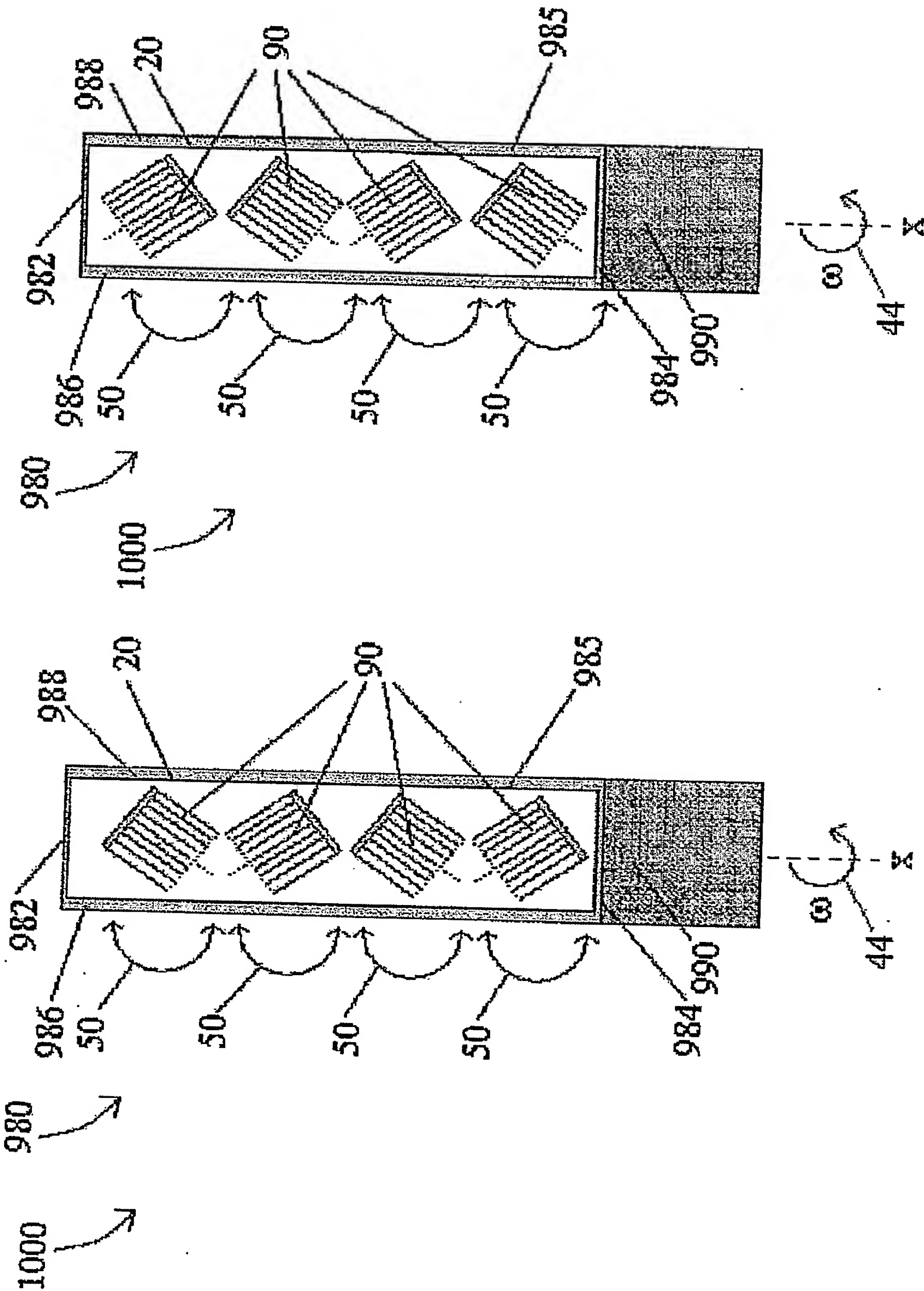


Fig. 63E

Fig. 63D

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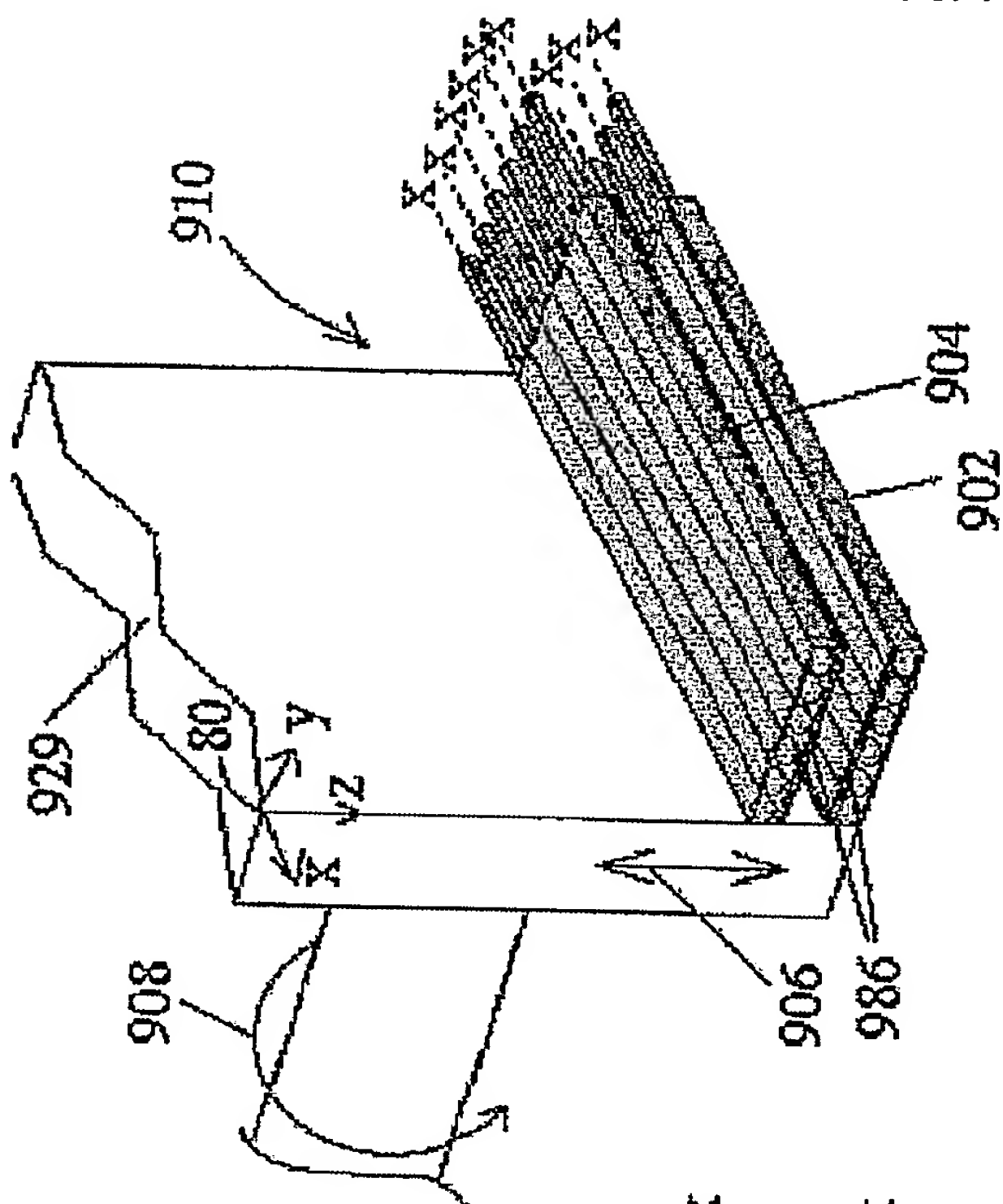


Fig. 64B

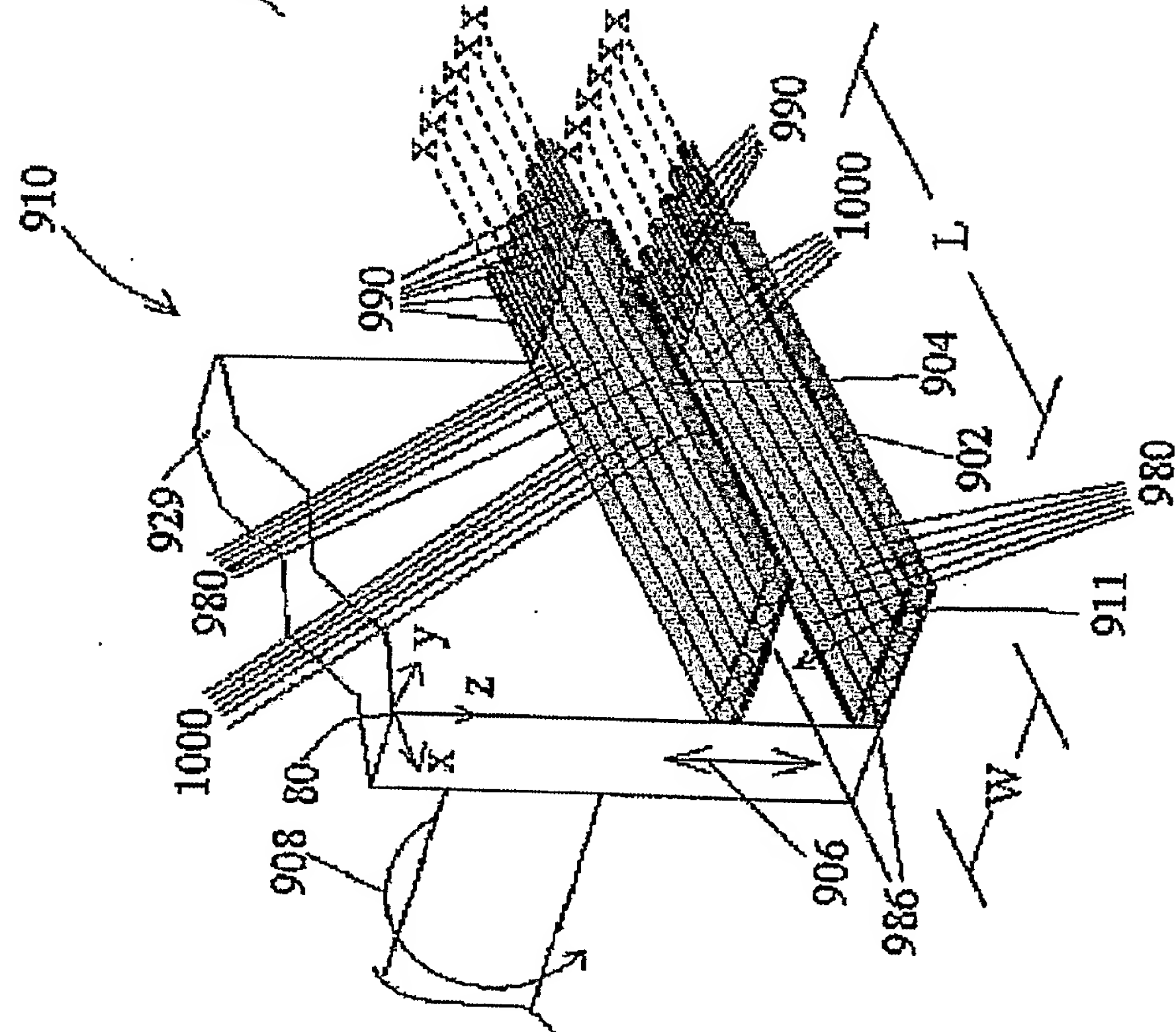


Fig. 64A

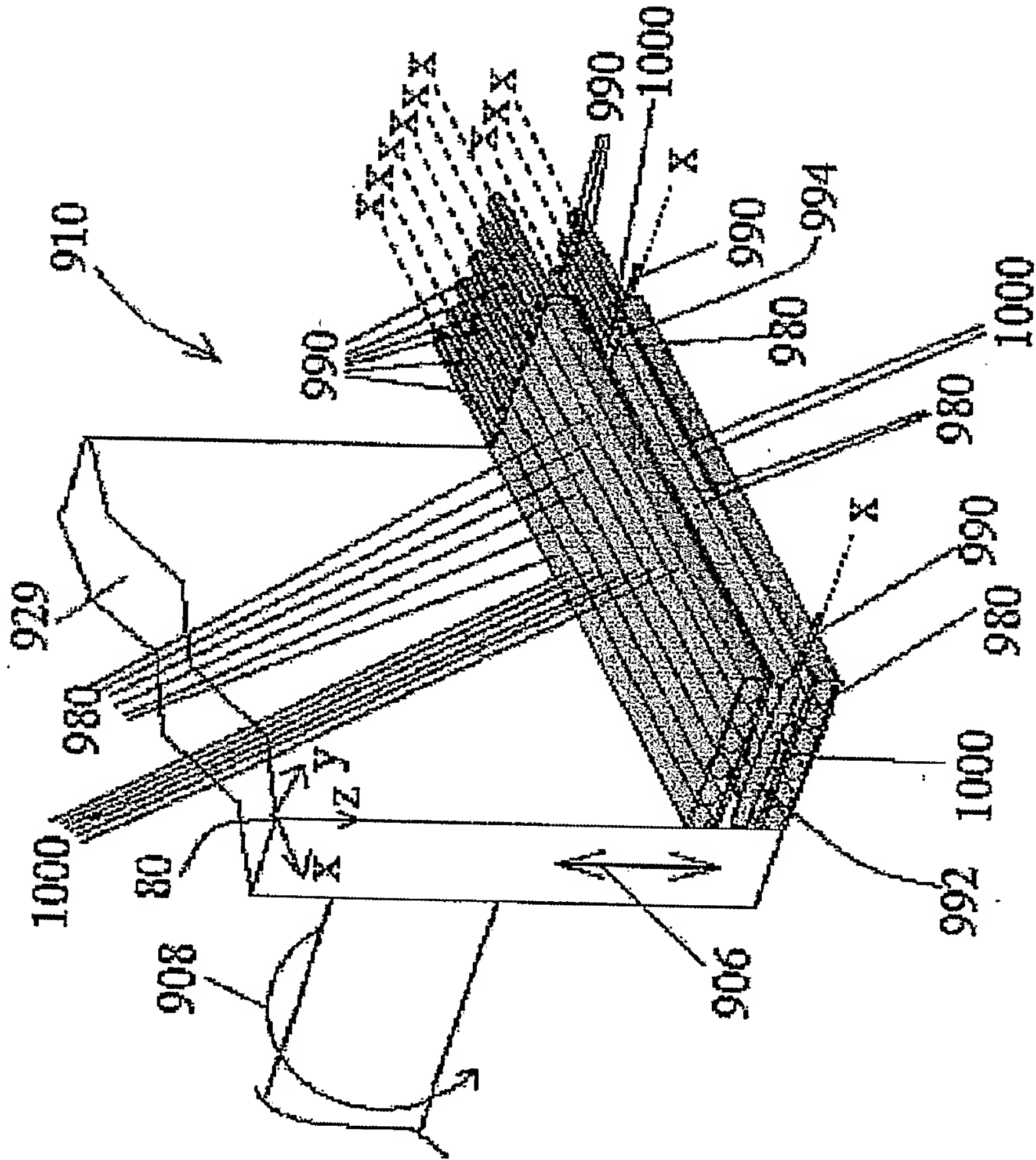


Fig. 64C

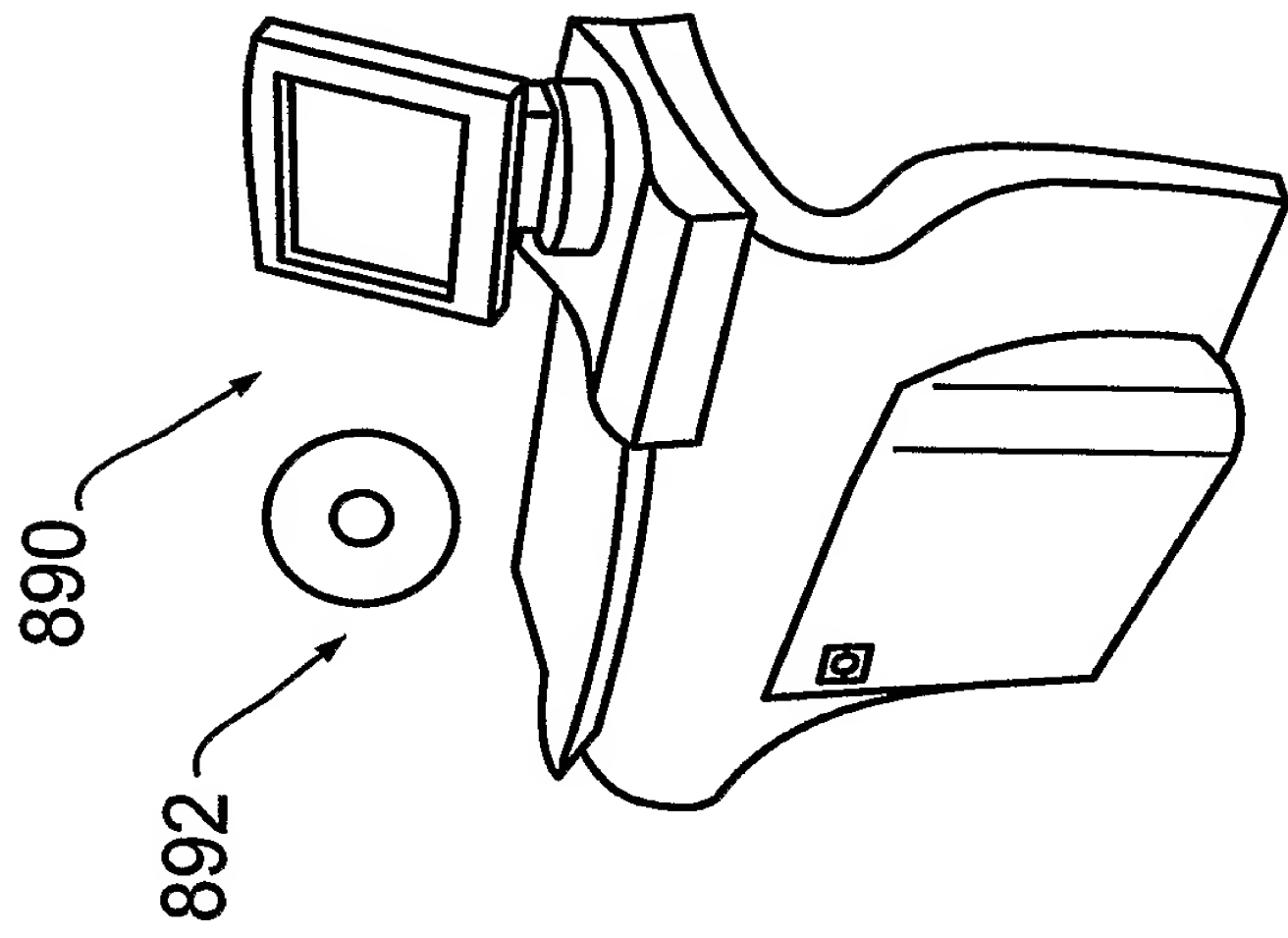


Fig. 64E

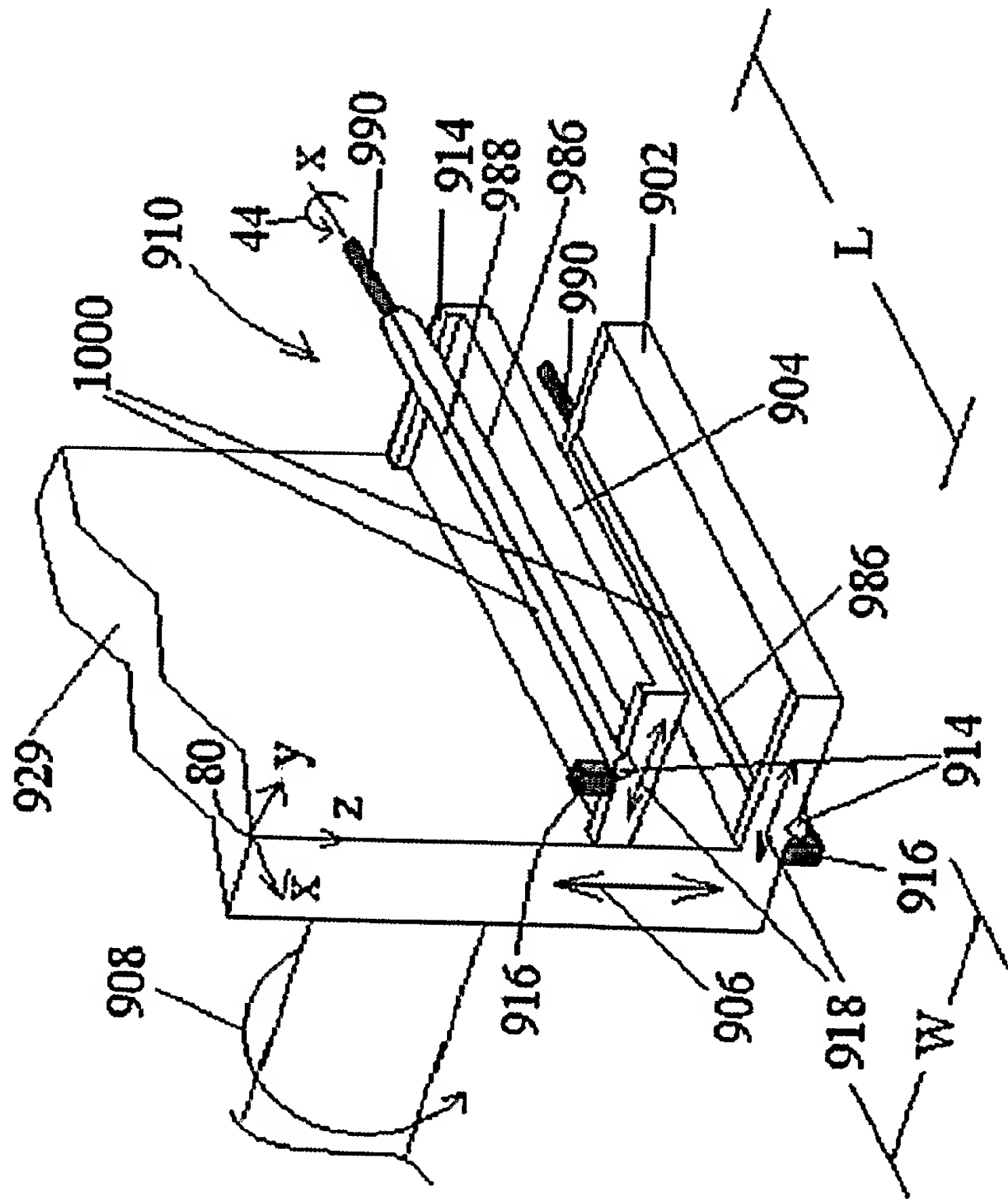


Fig. 64D

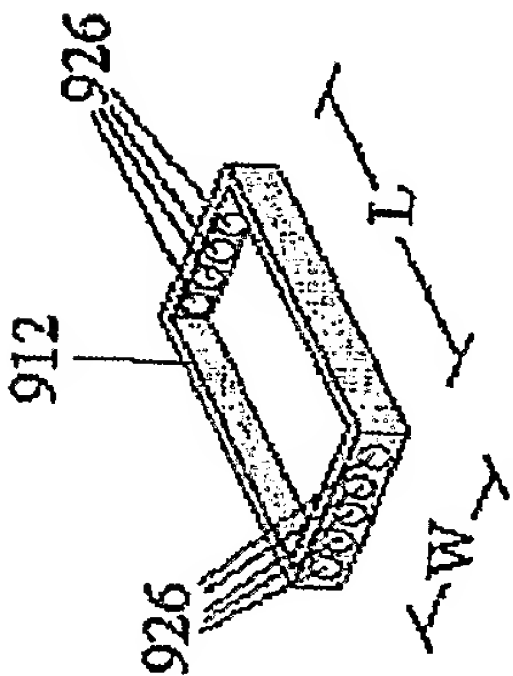


Fig. 64F

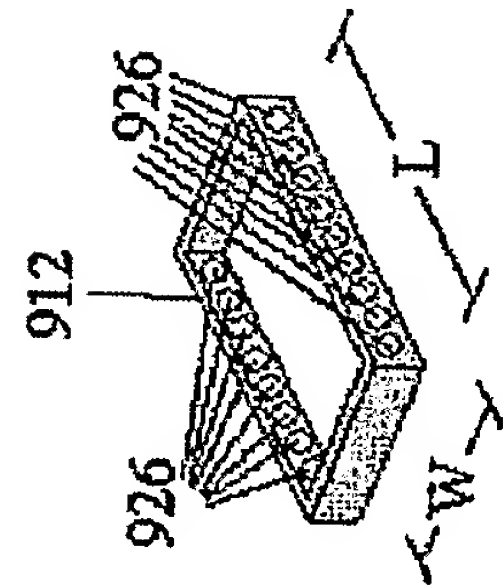


Fig. 64G

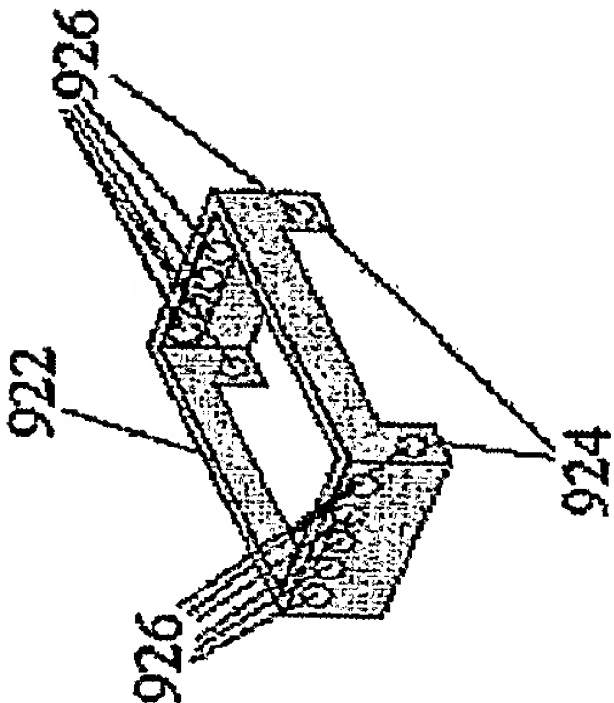


Fig. 64H

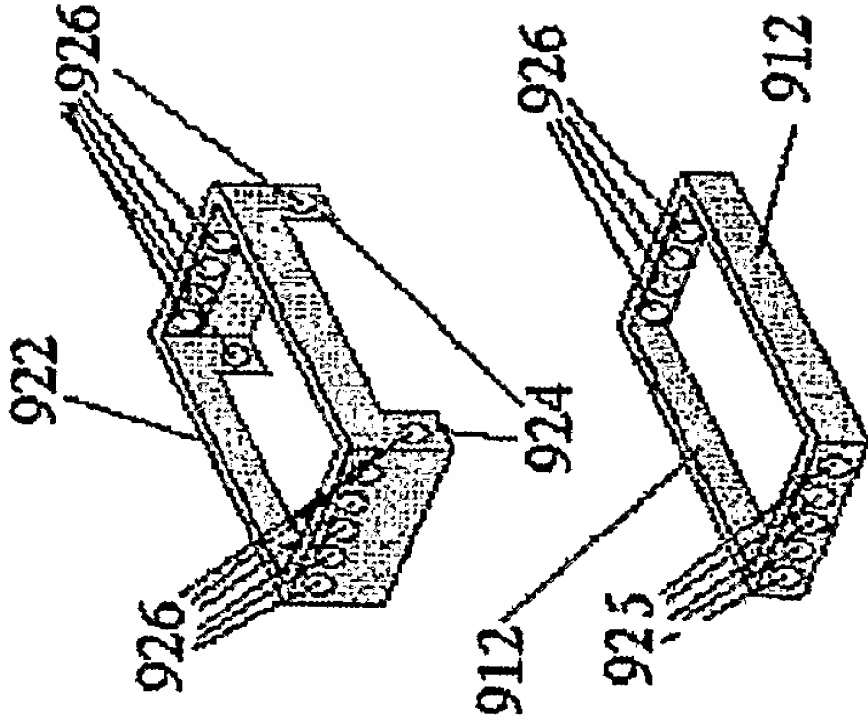


Fig. 64I

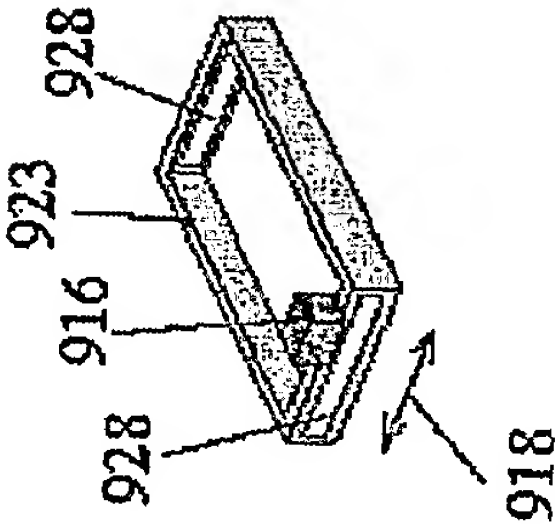


Fig. 64J

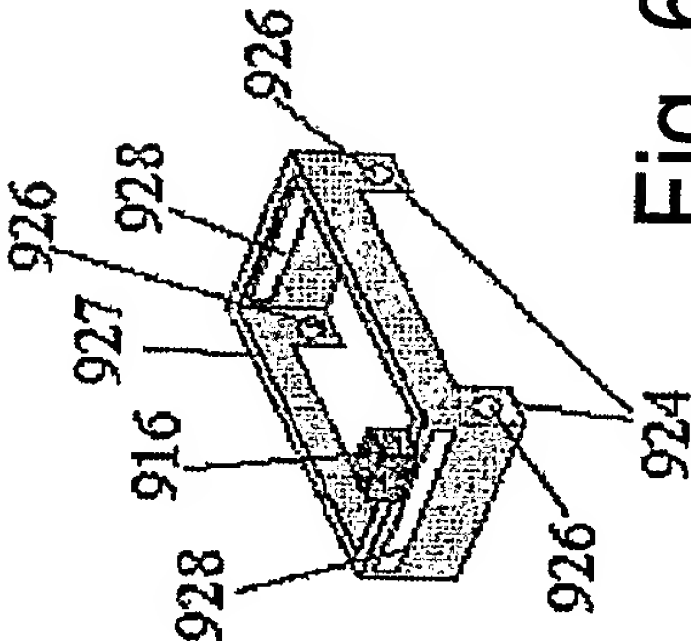
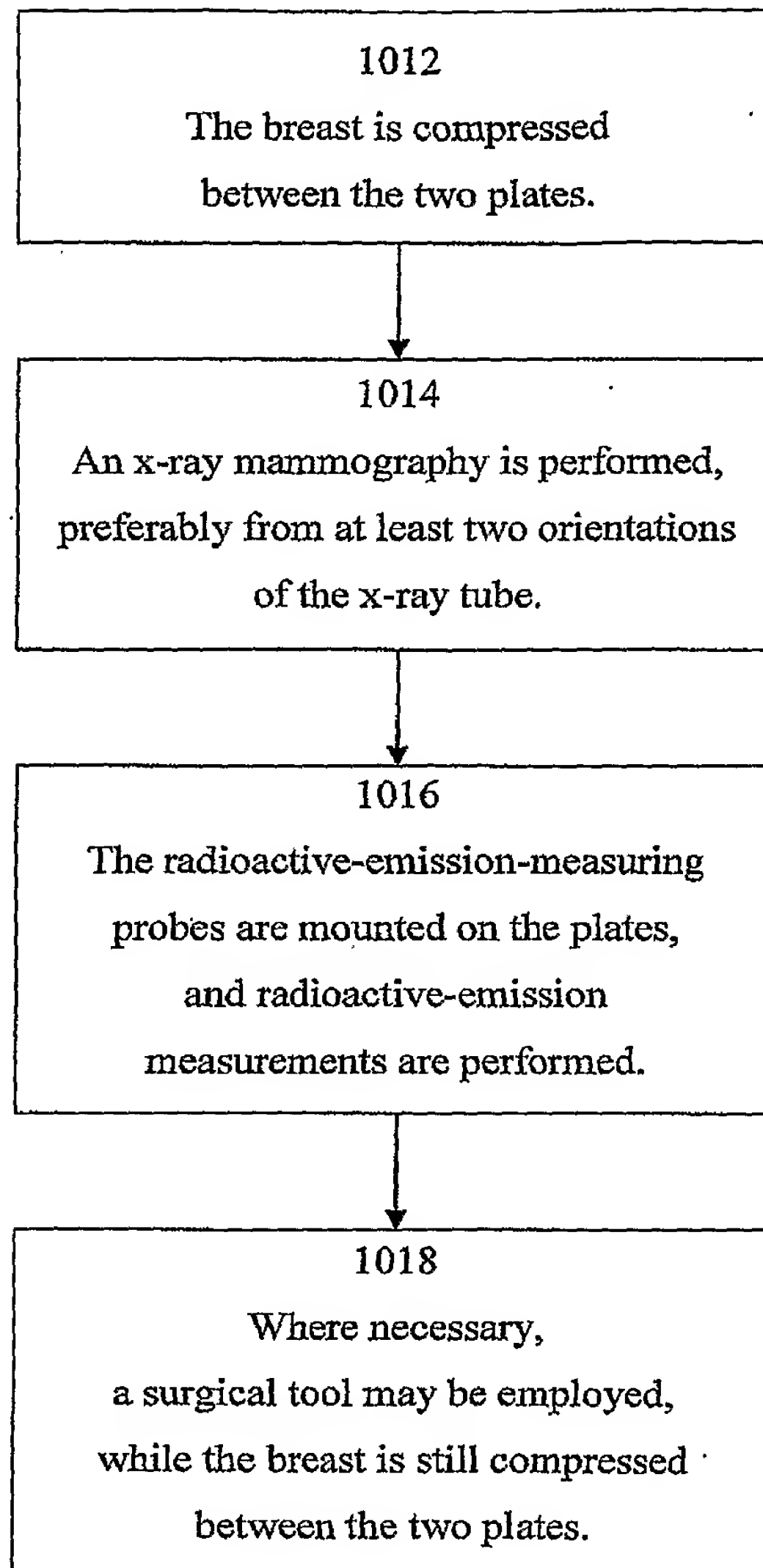


Fig. 64K

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**Figure 64L**

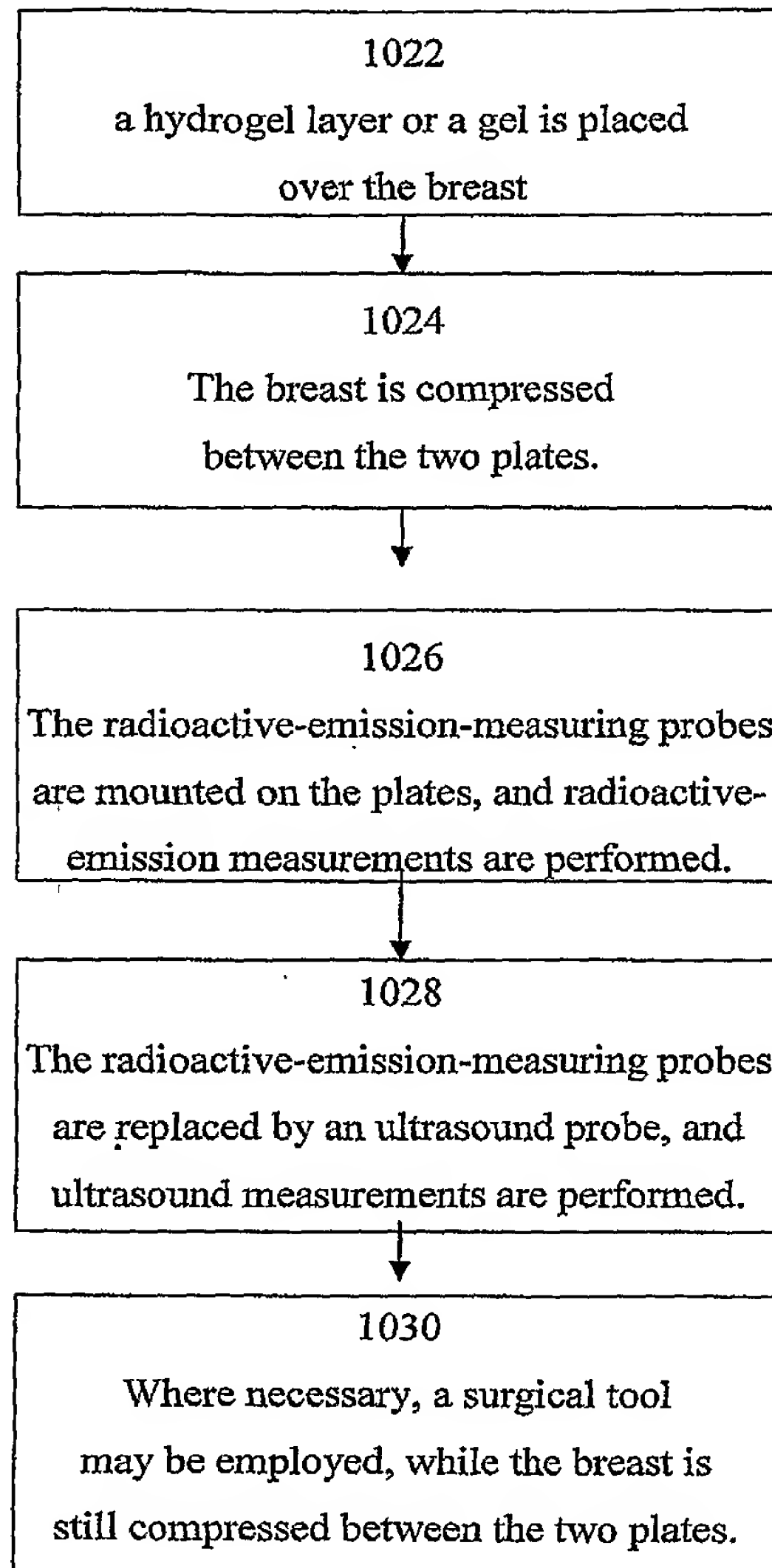
1010



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**Figure 64M**

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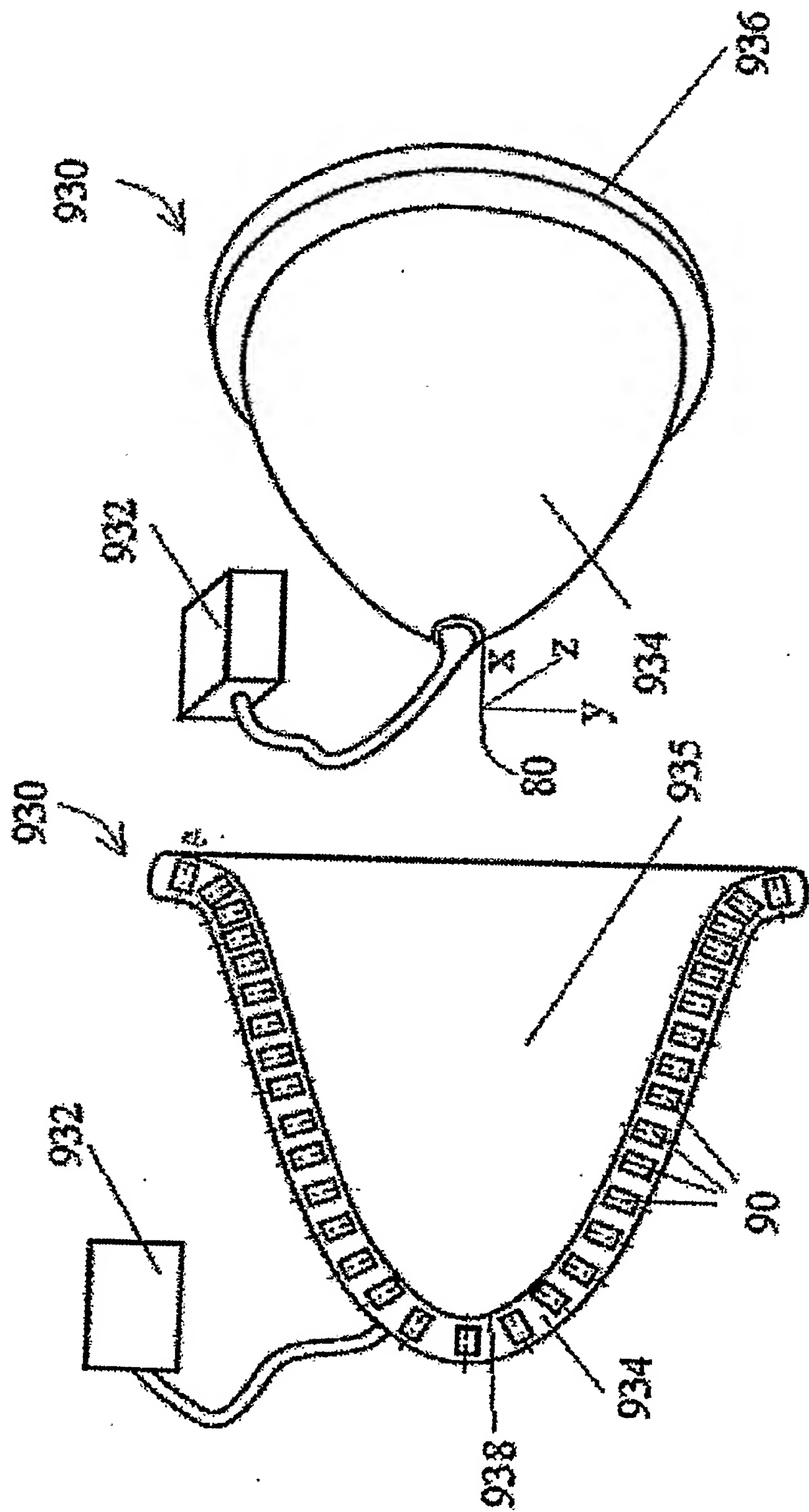


Fig. 65A

Fig. 65B

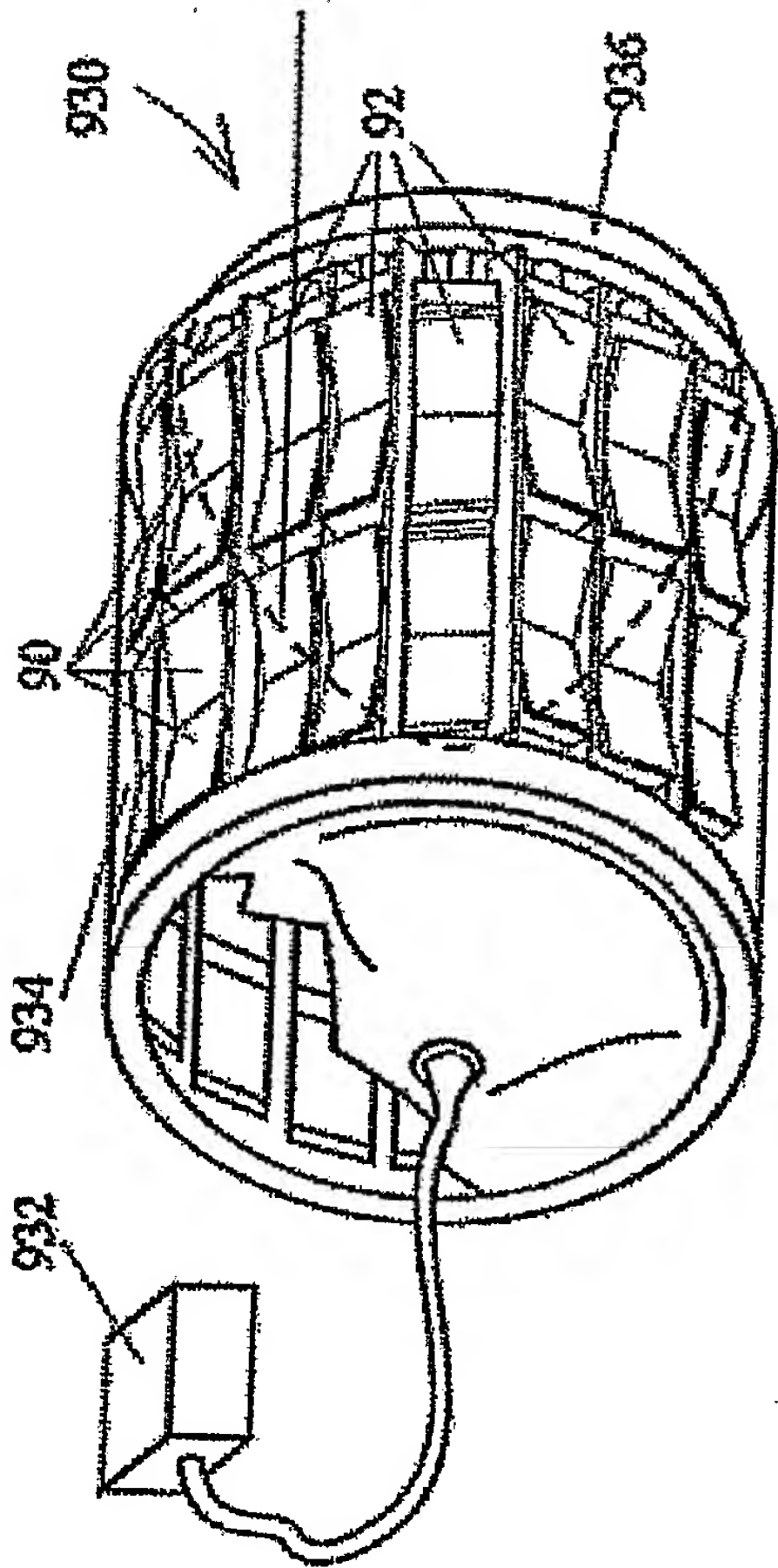
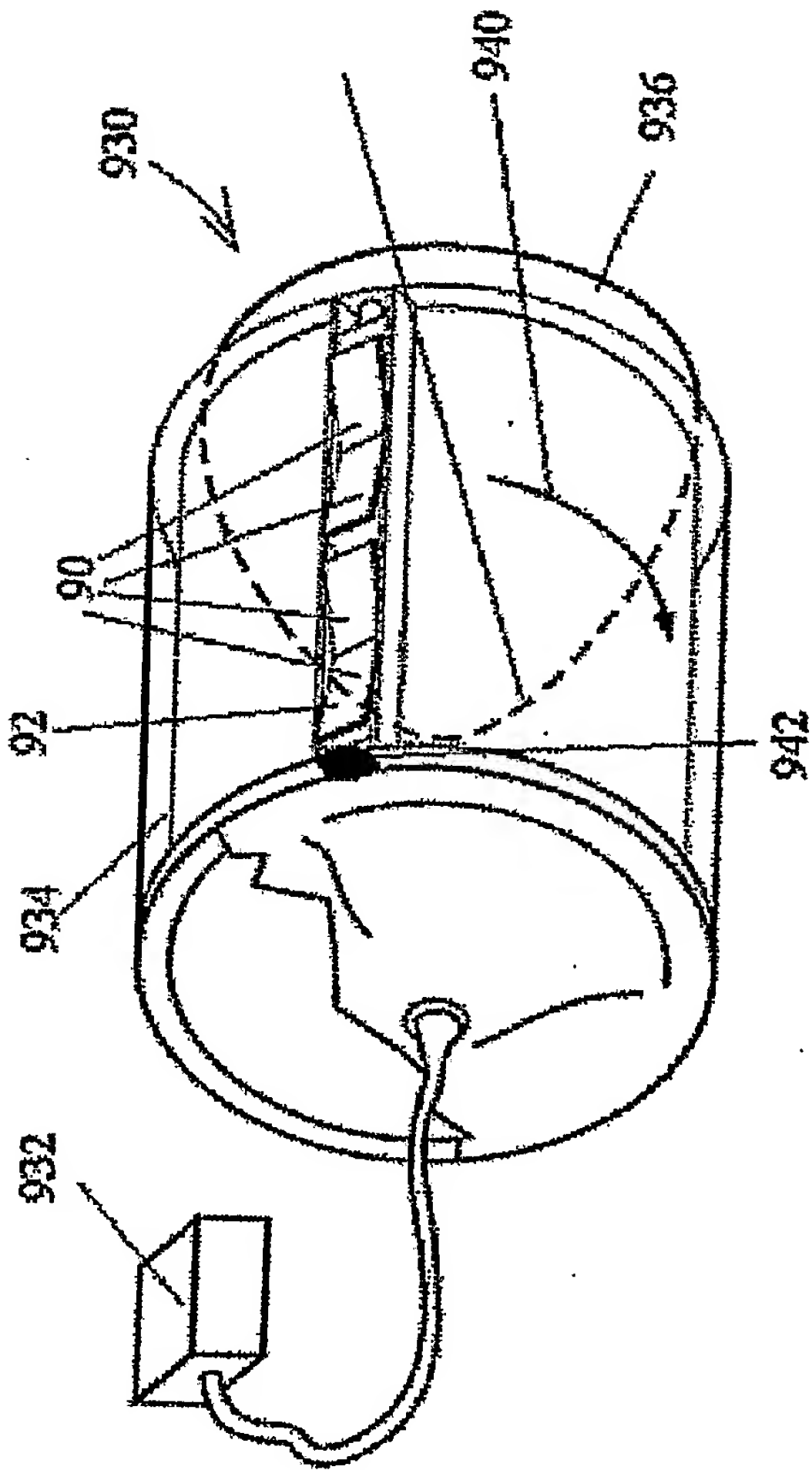


Fig. 65C



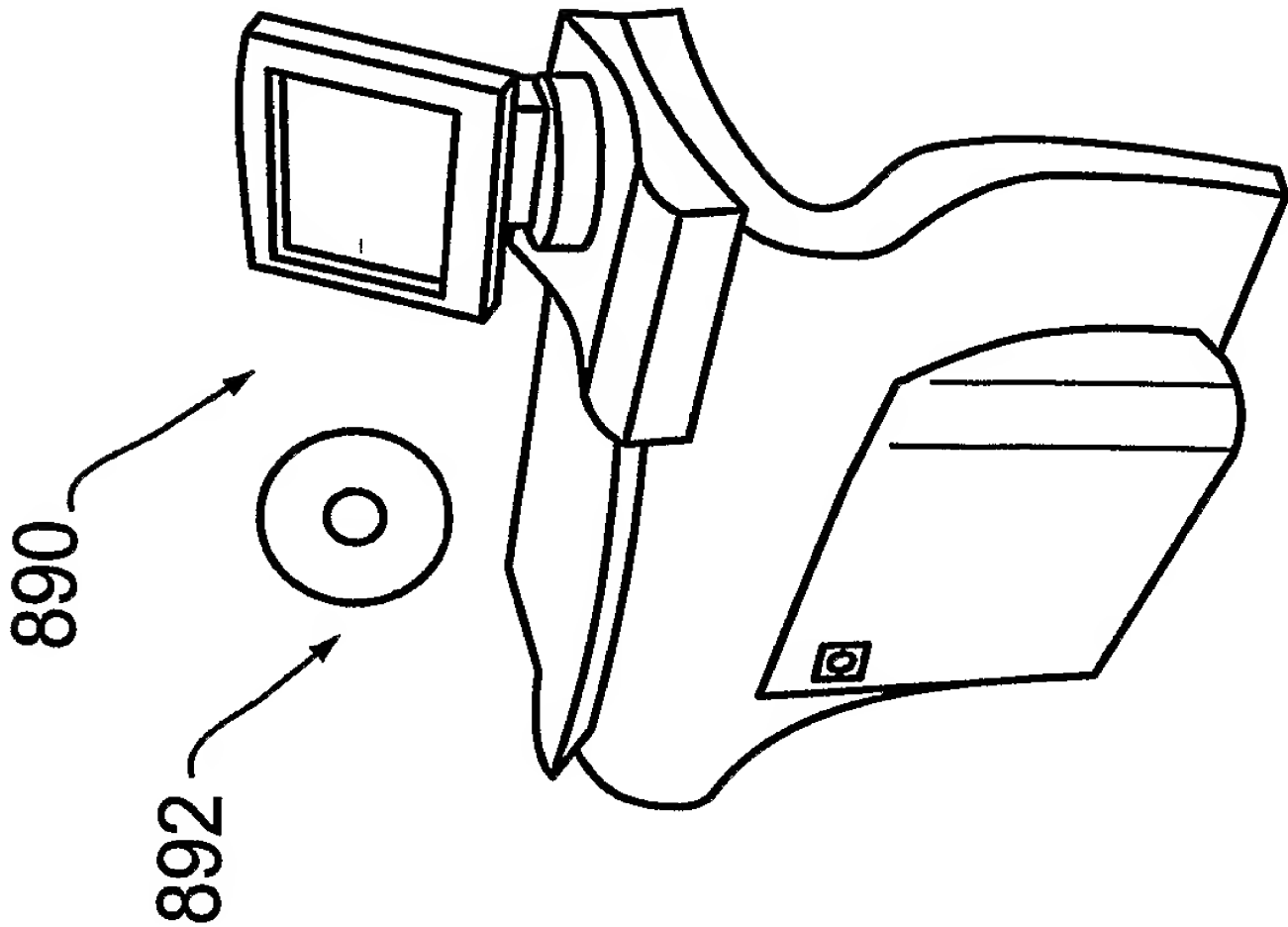


Fig. 66C

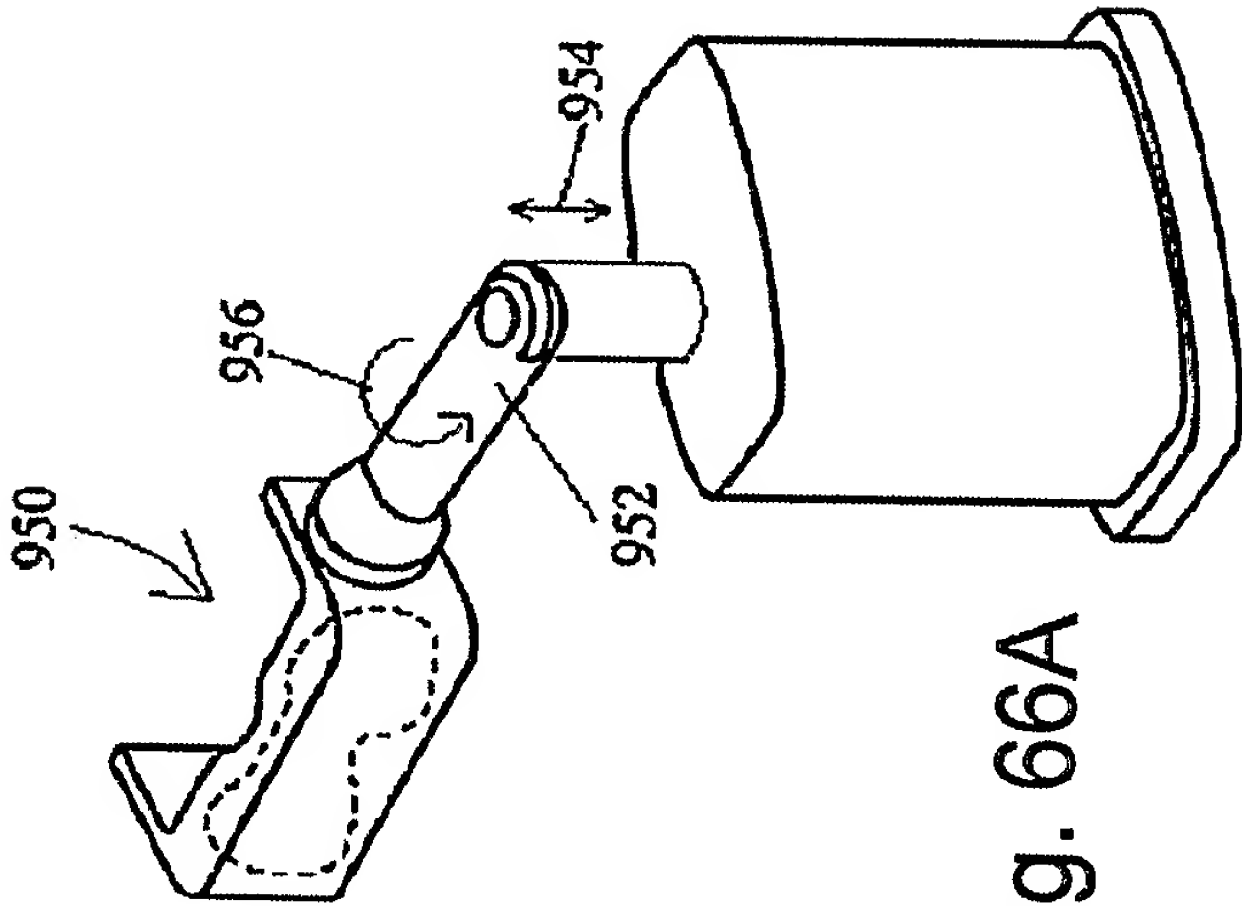


Fig. 66A

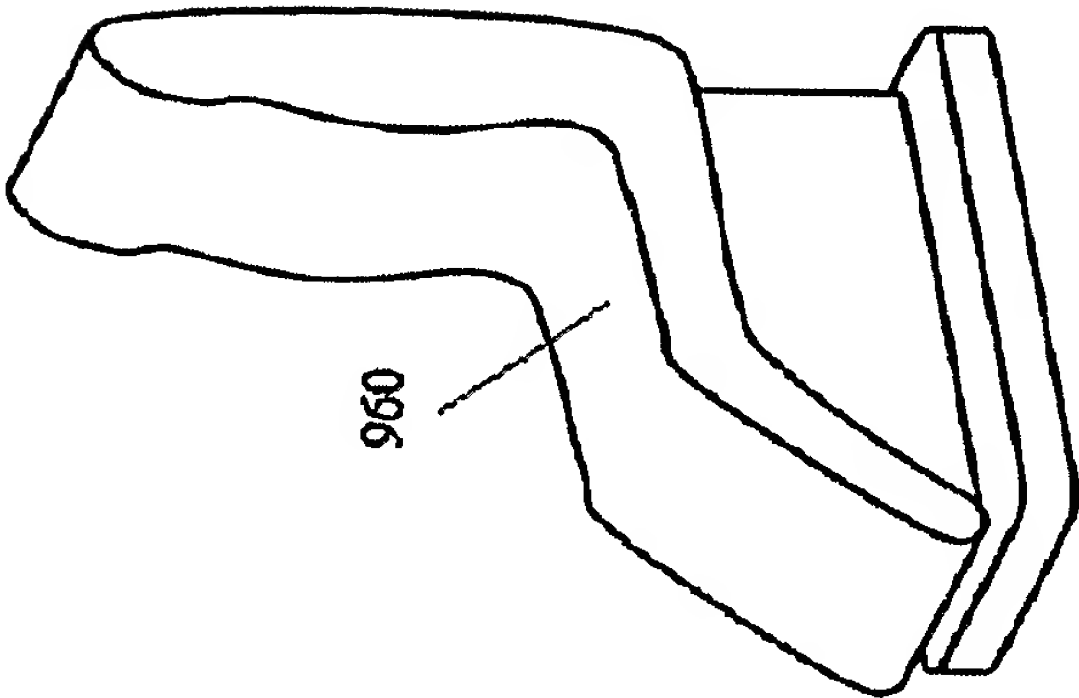


Fig. 66B

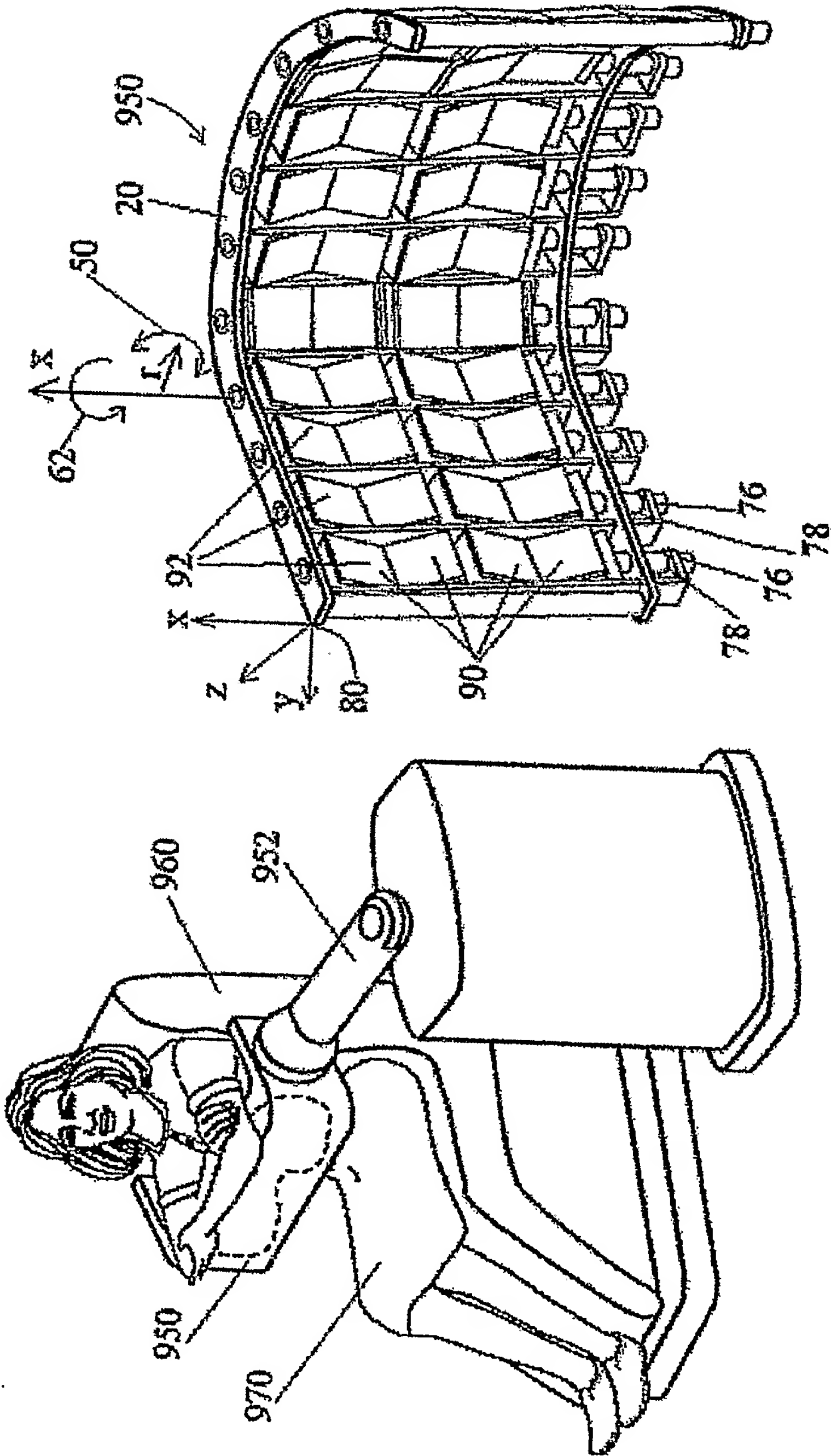


Fig. 66E

Fig. 66D

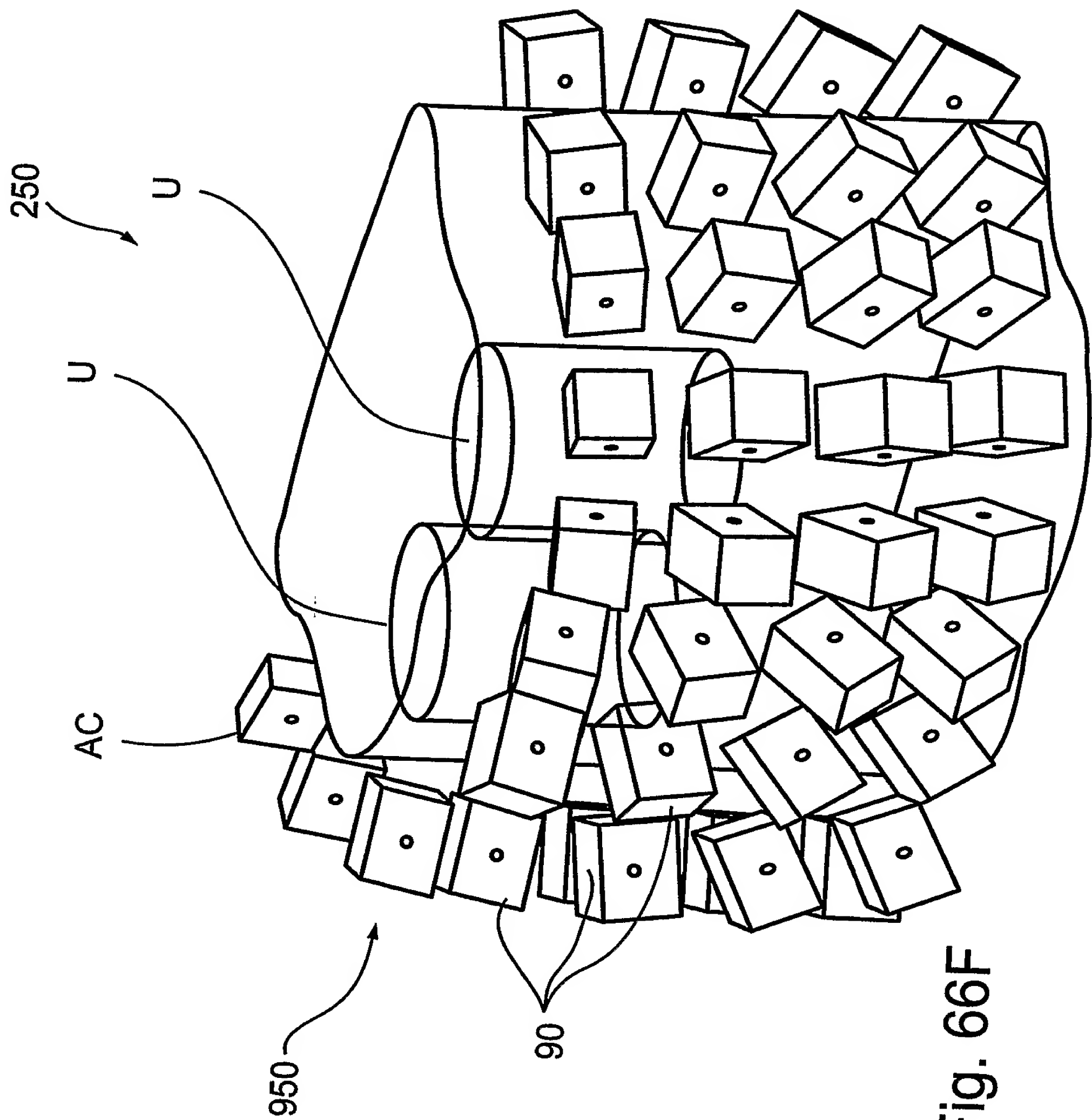


Fig. 66F

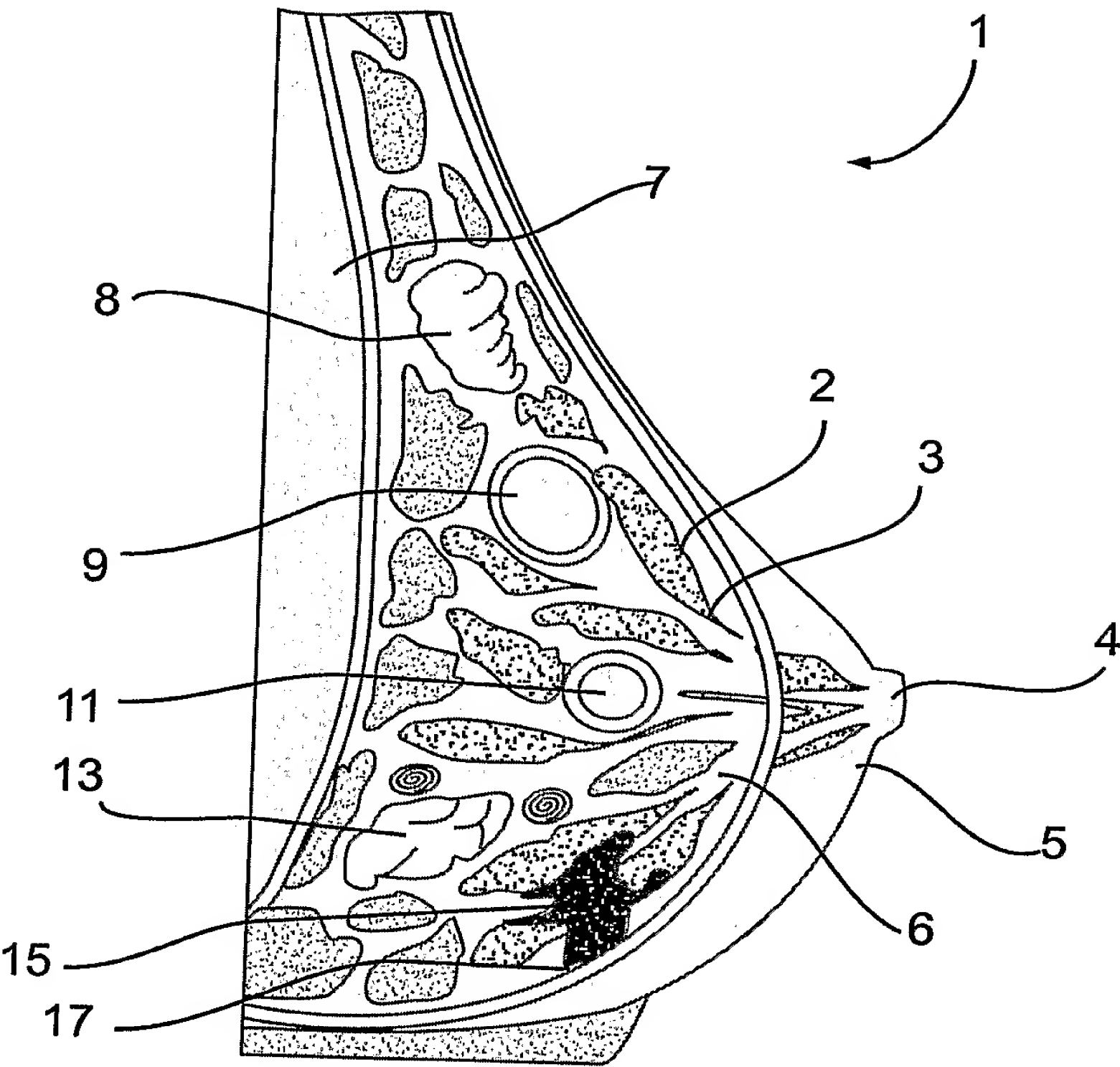


Fig. 66G

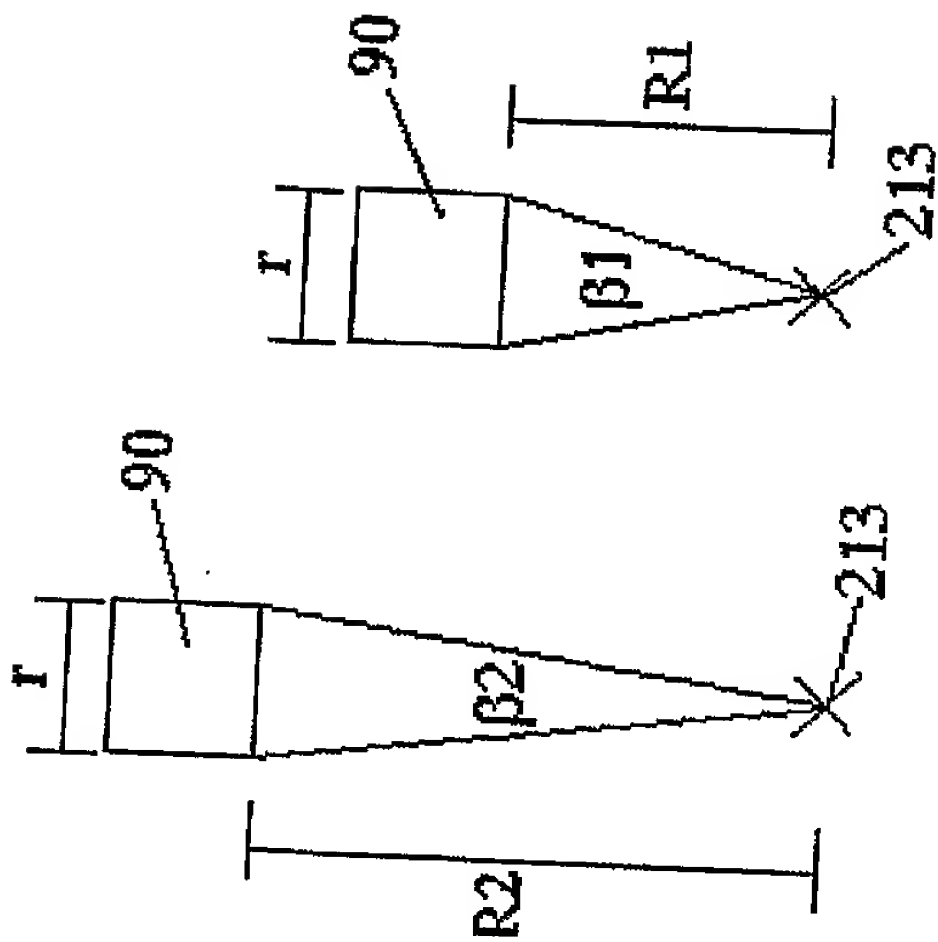
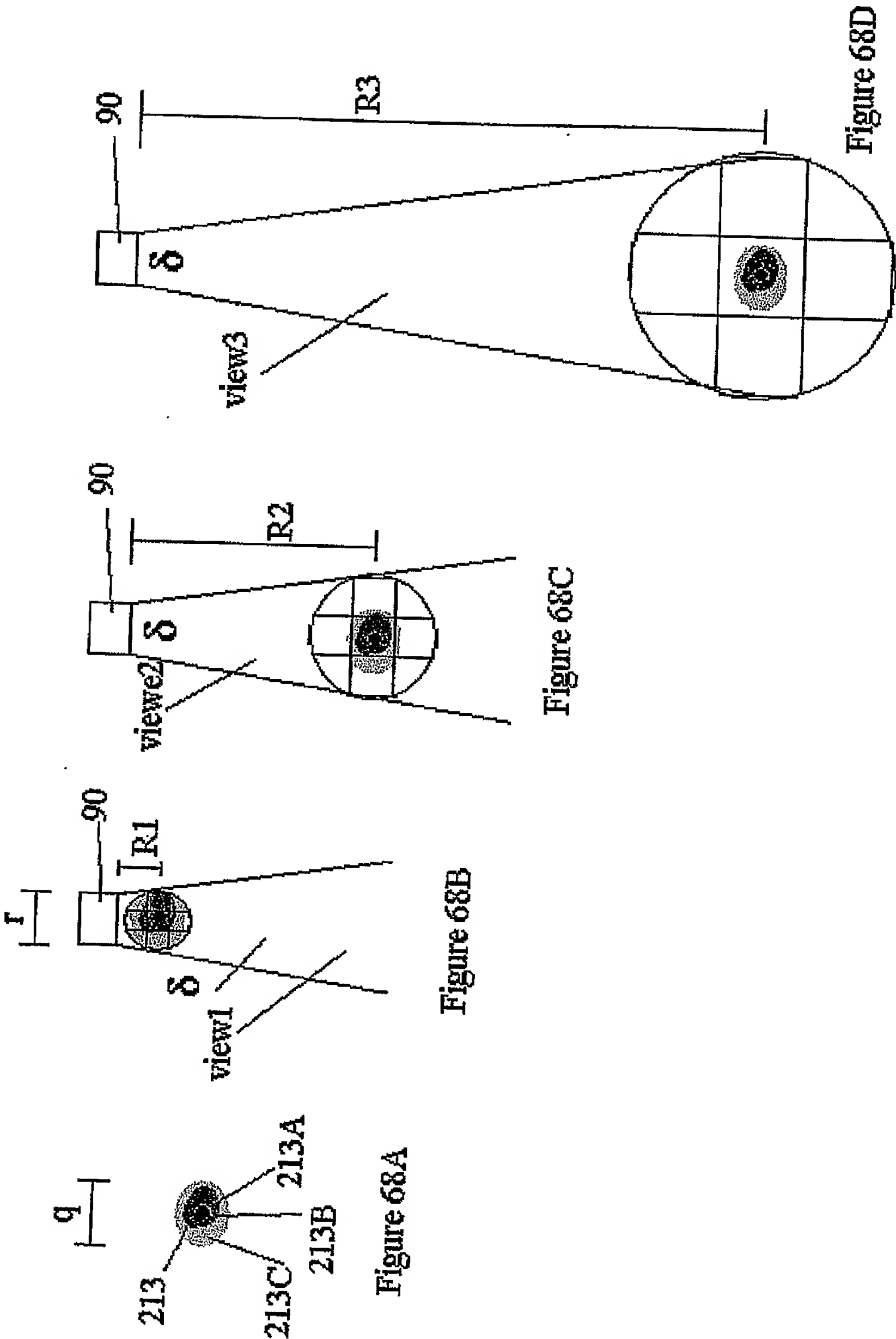


Figure 67A

Figure 67B





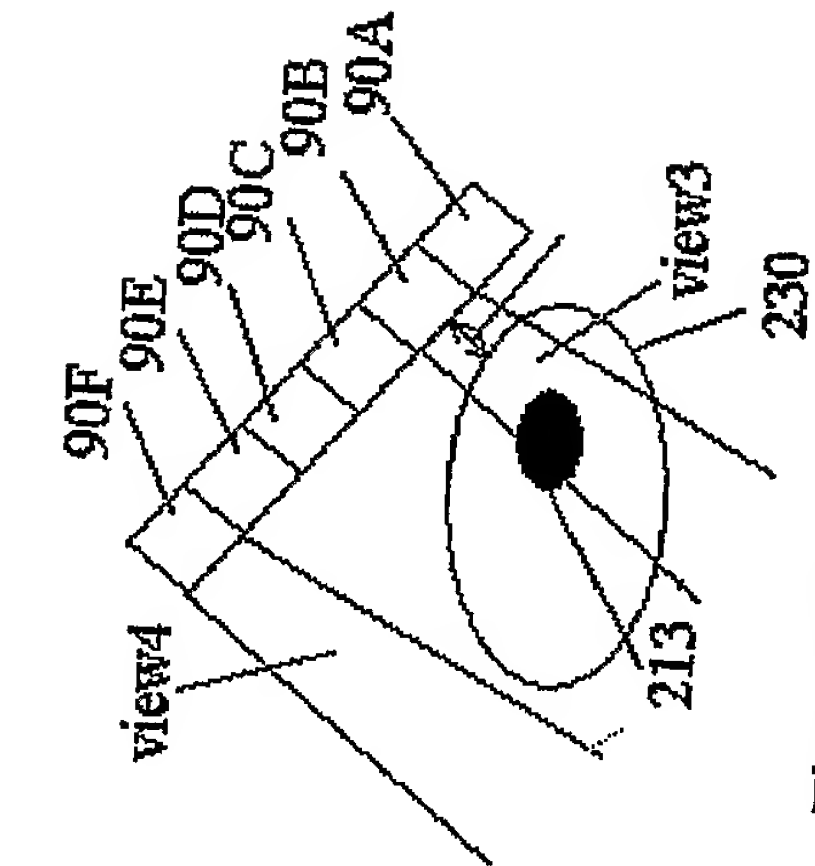


Figure 69B

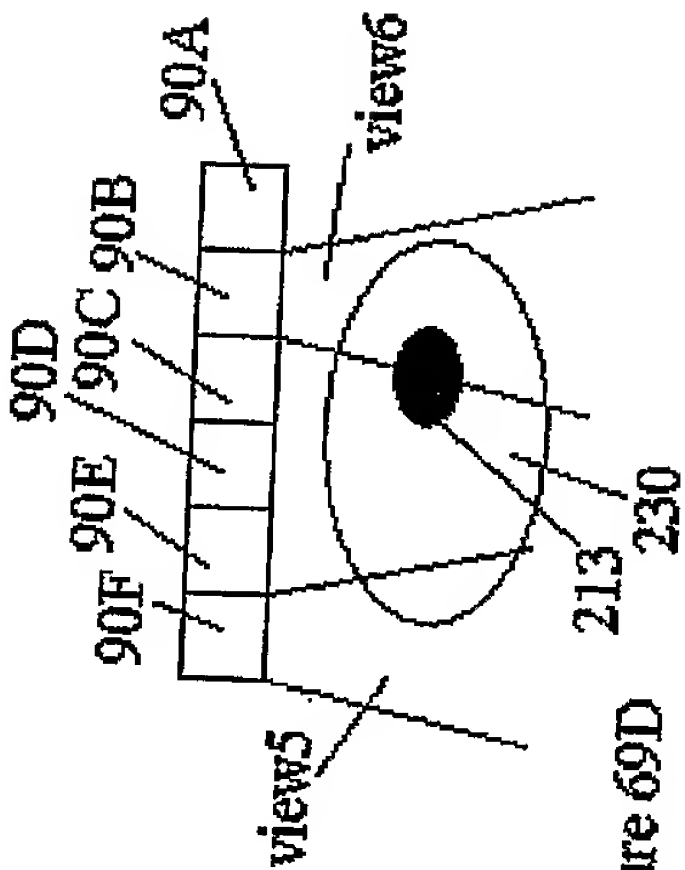


Figure 69D

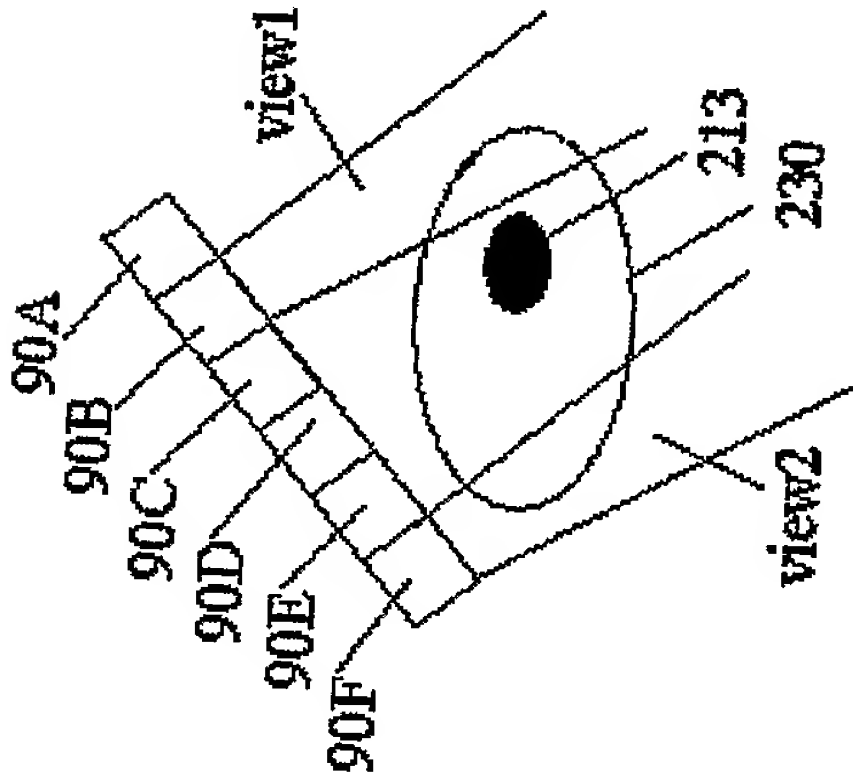


Figure 69C

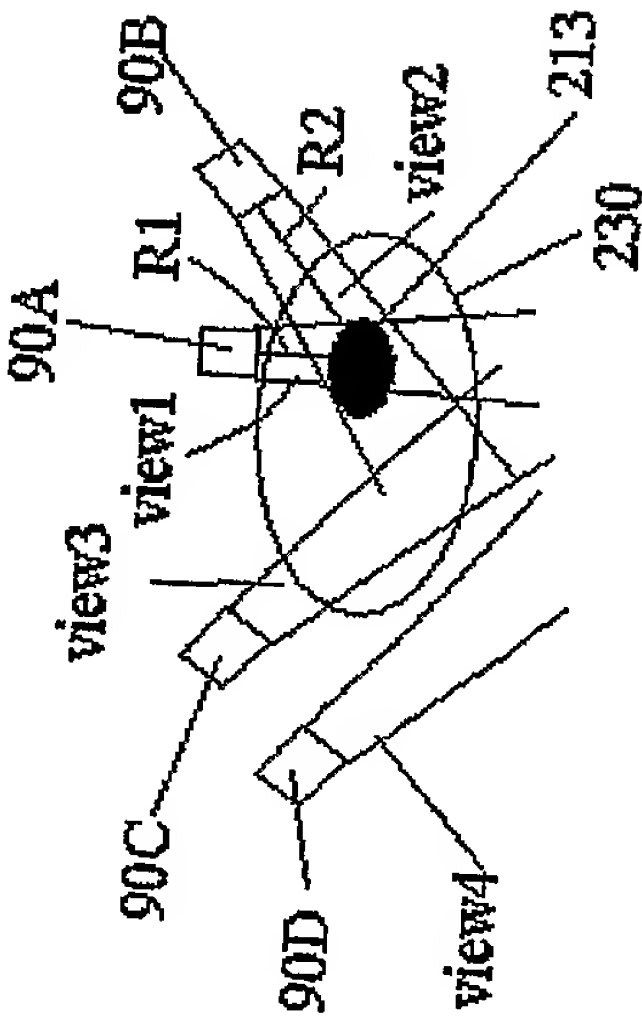


Figure 69A

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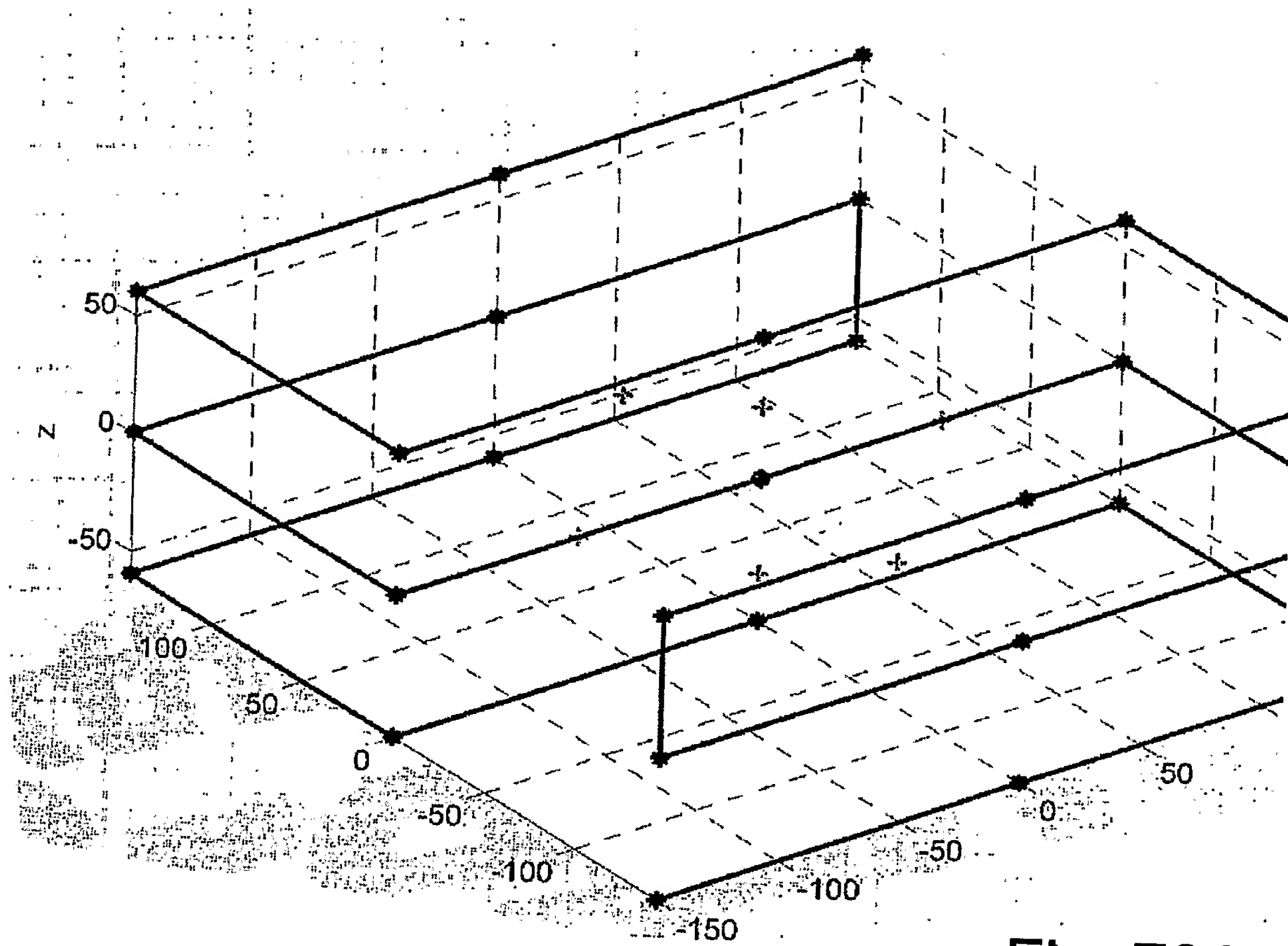


Fig. 70A

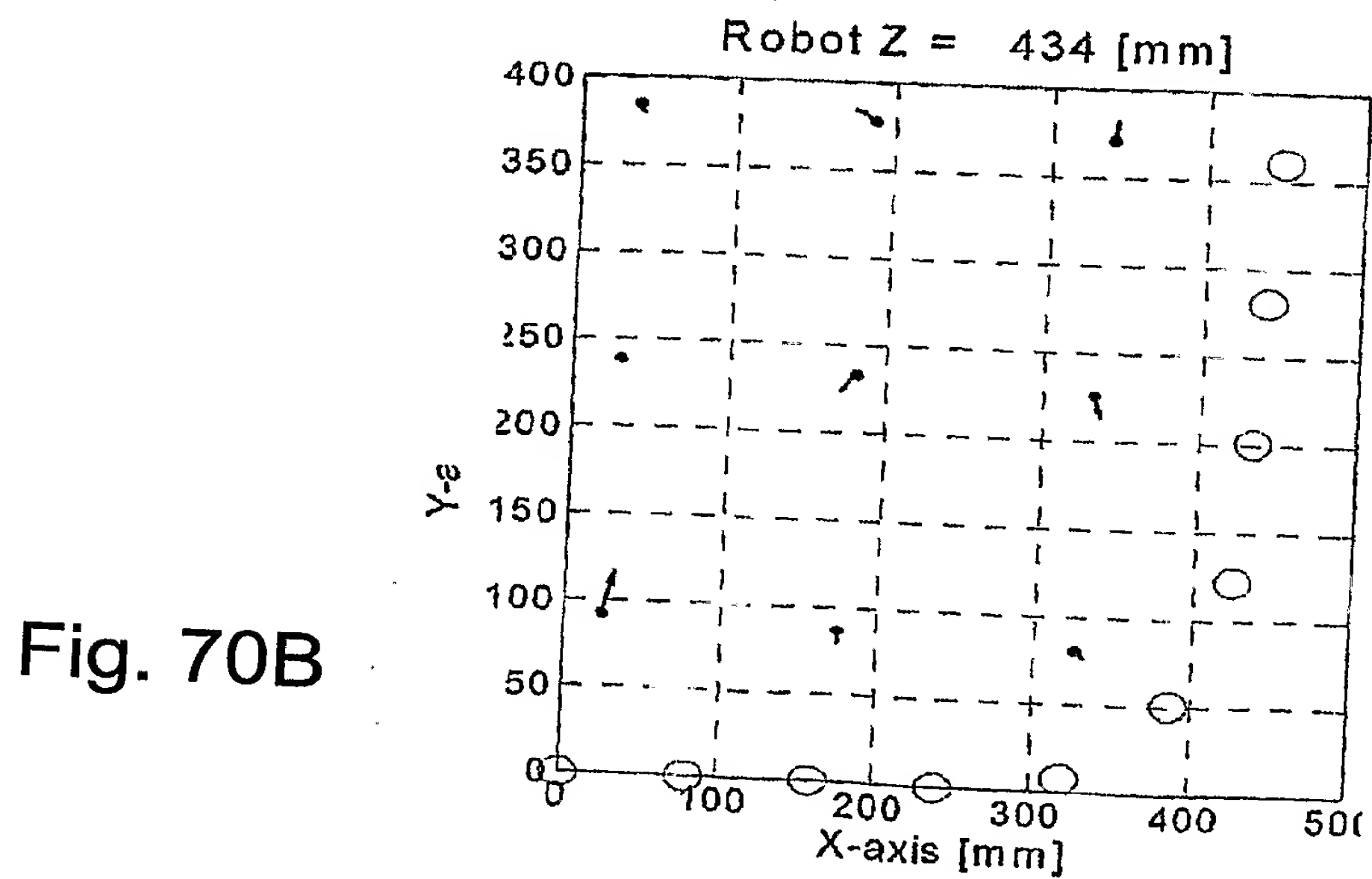


Fig. 70B

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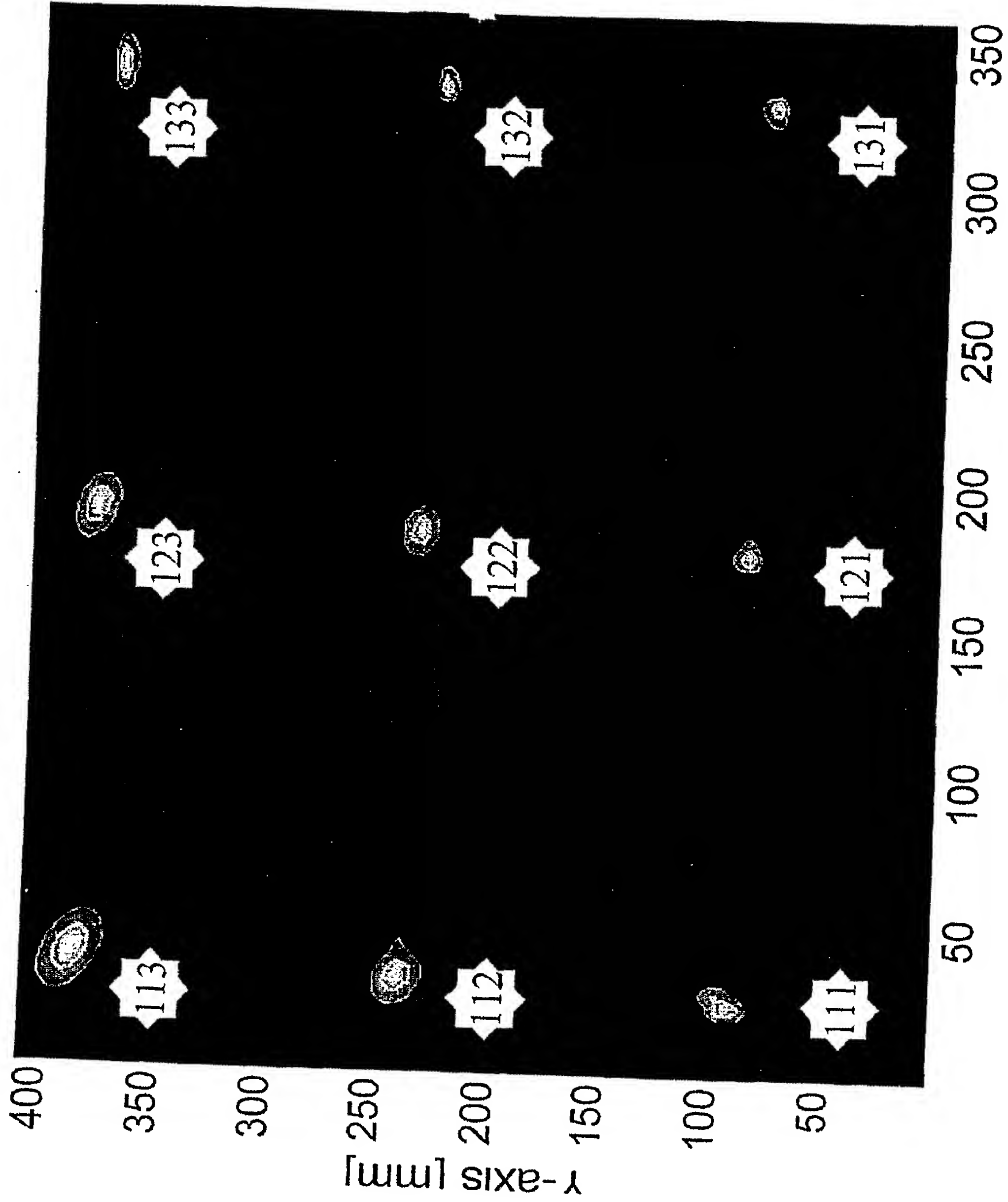
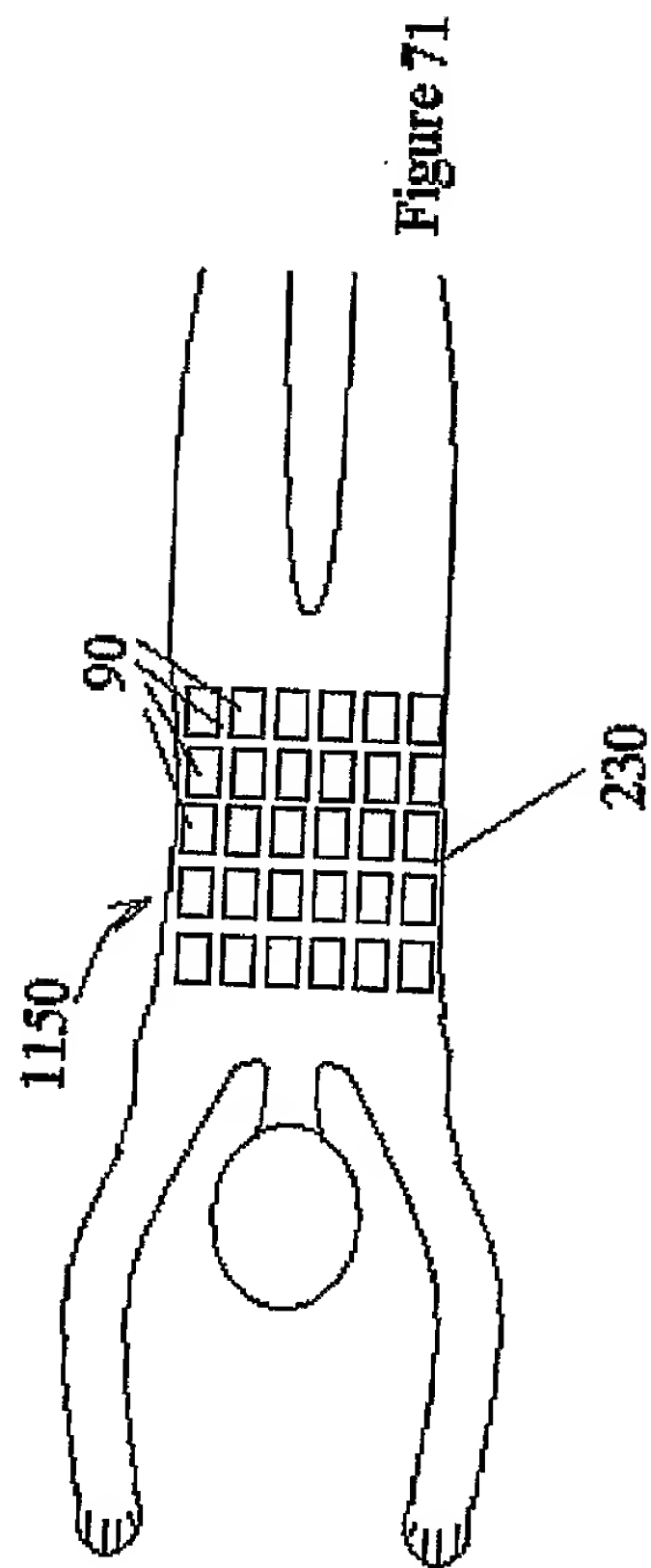
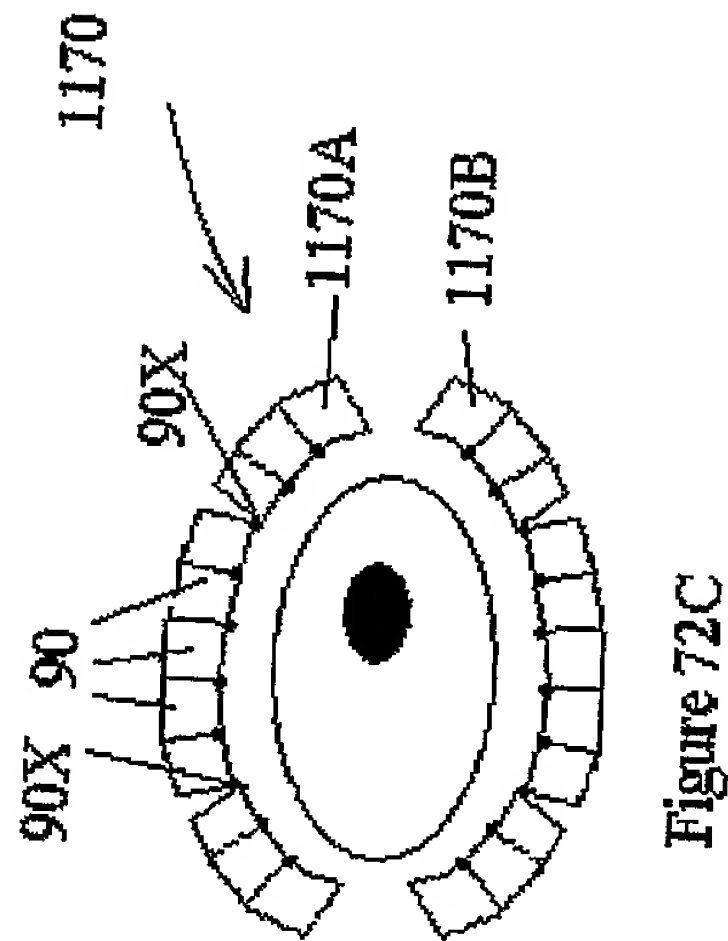
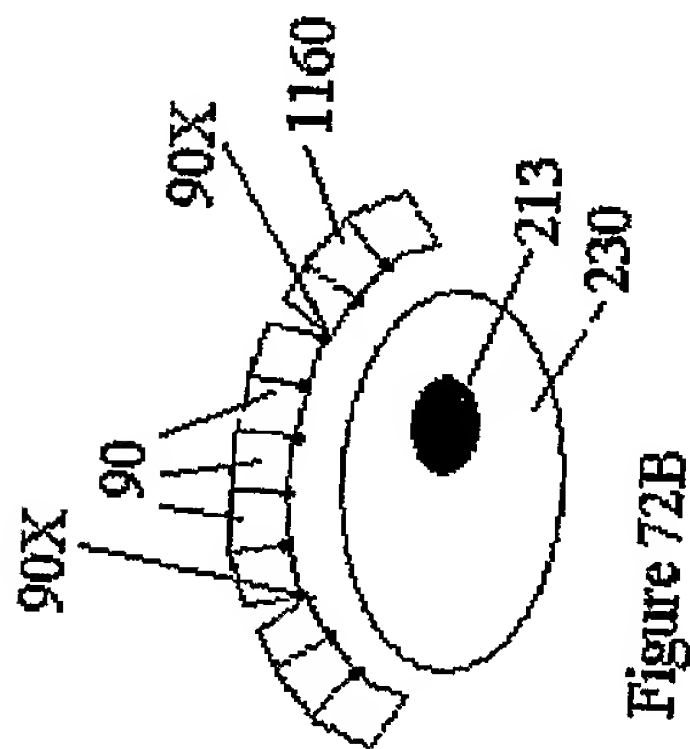
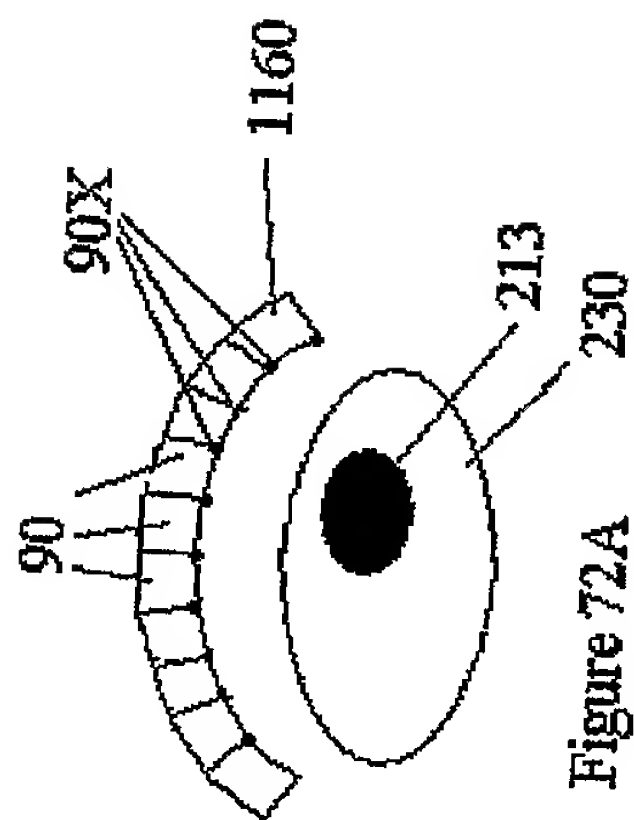


Fig. 70C

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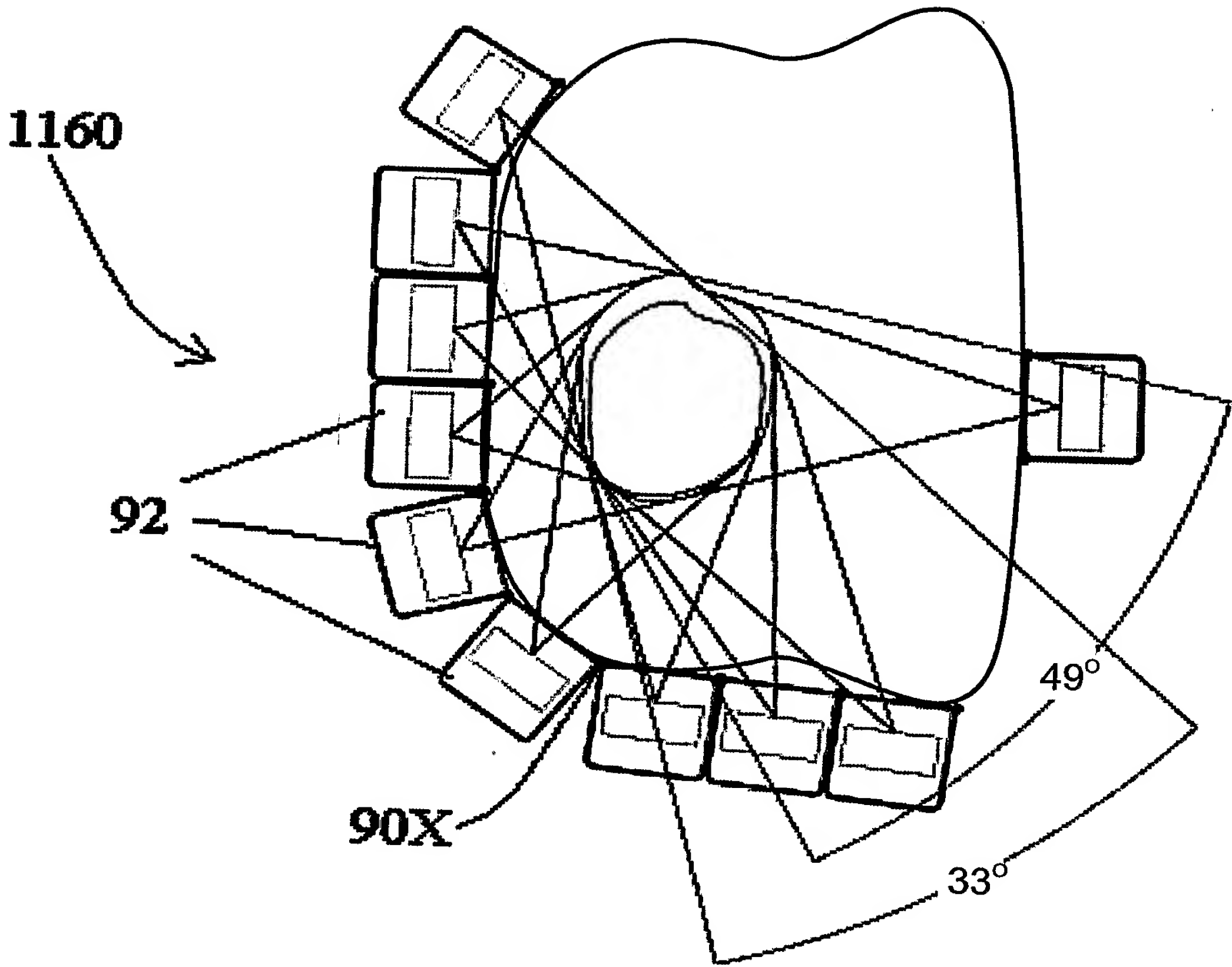


Fig. 72D

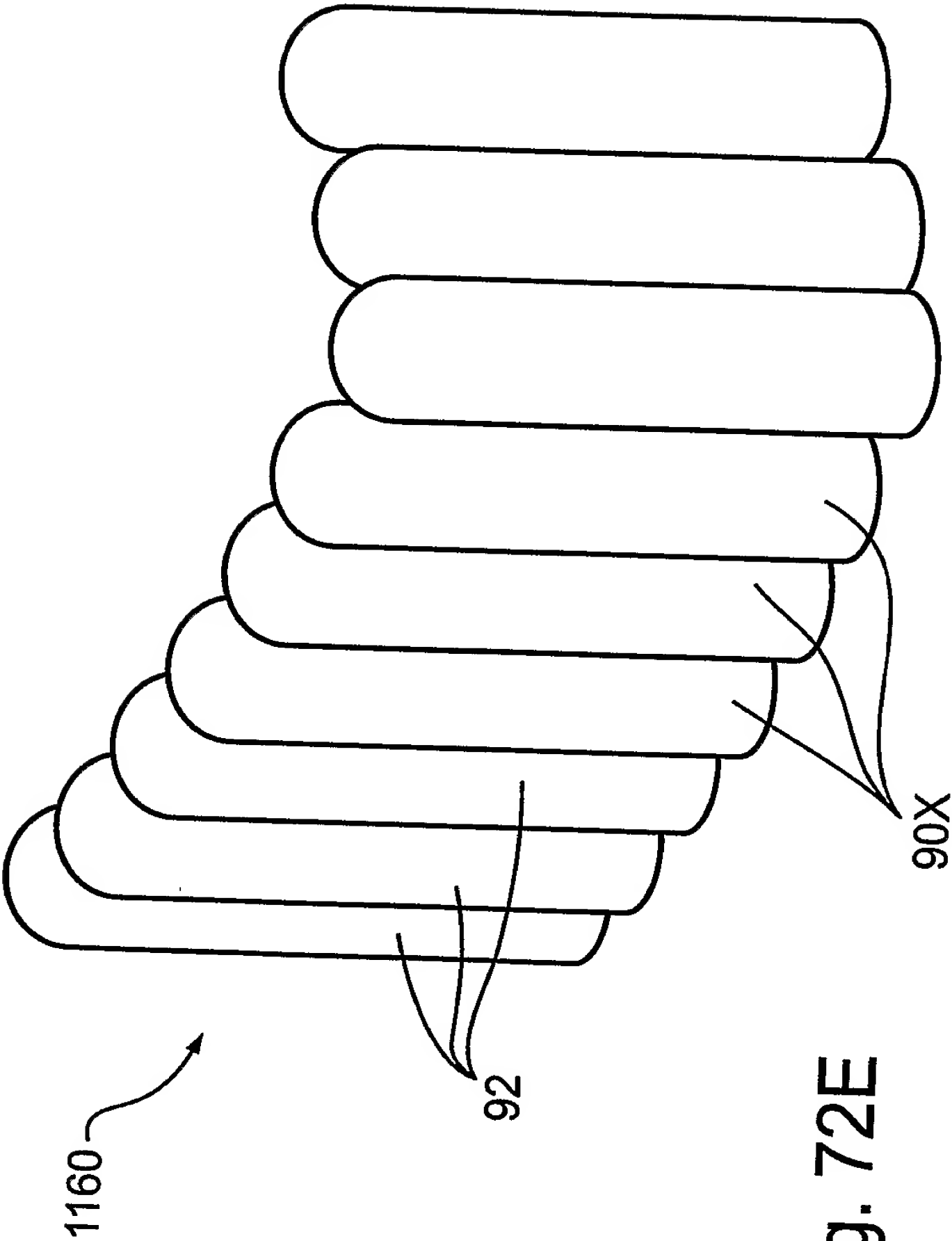


Fig. 72E

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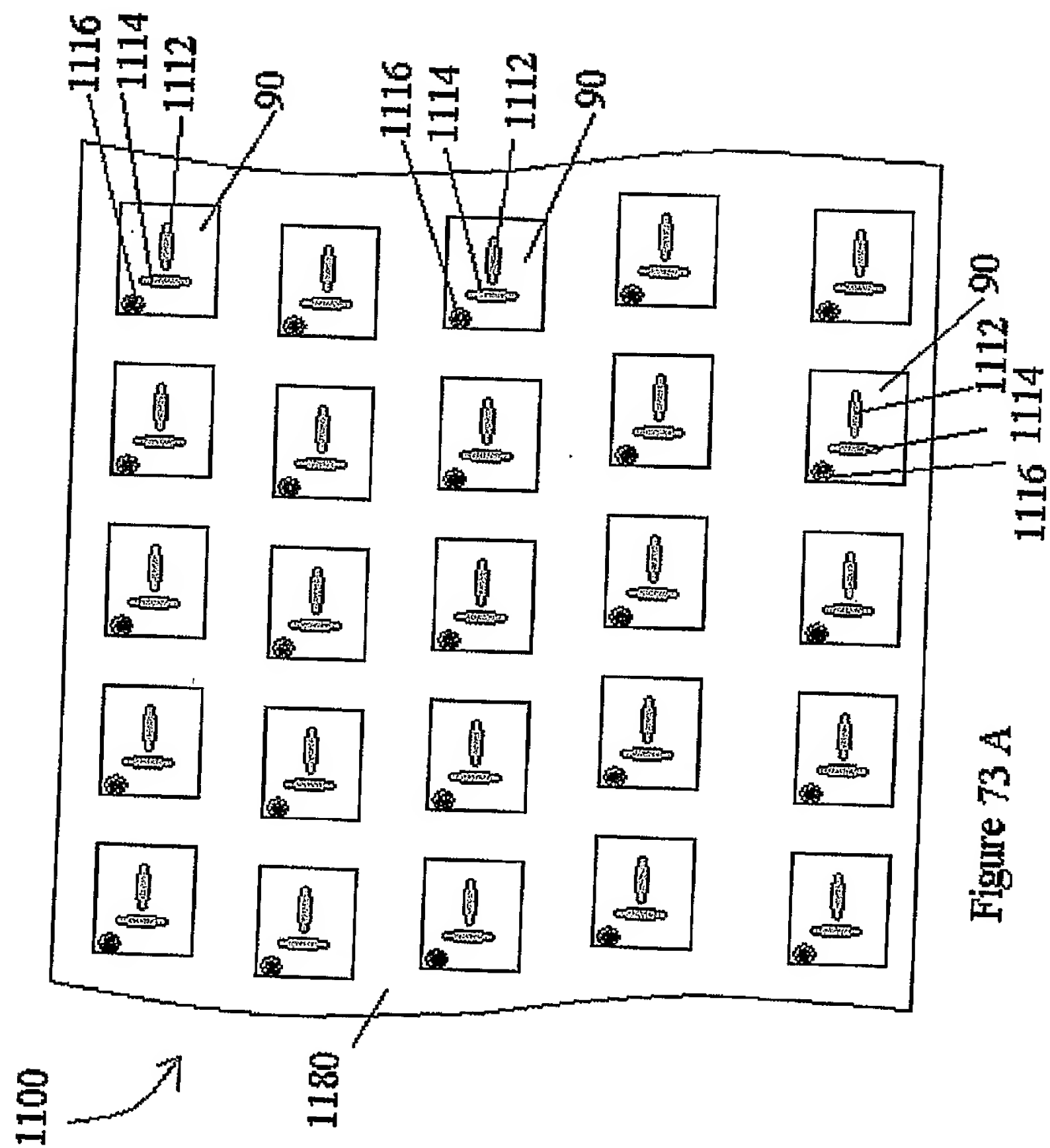


Figure 73 A



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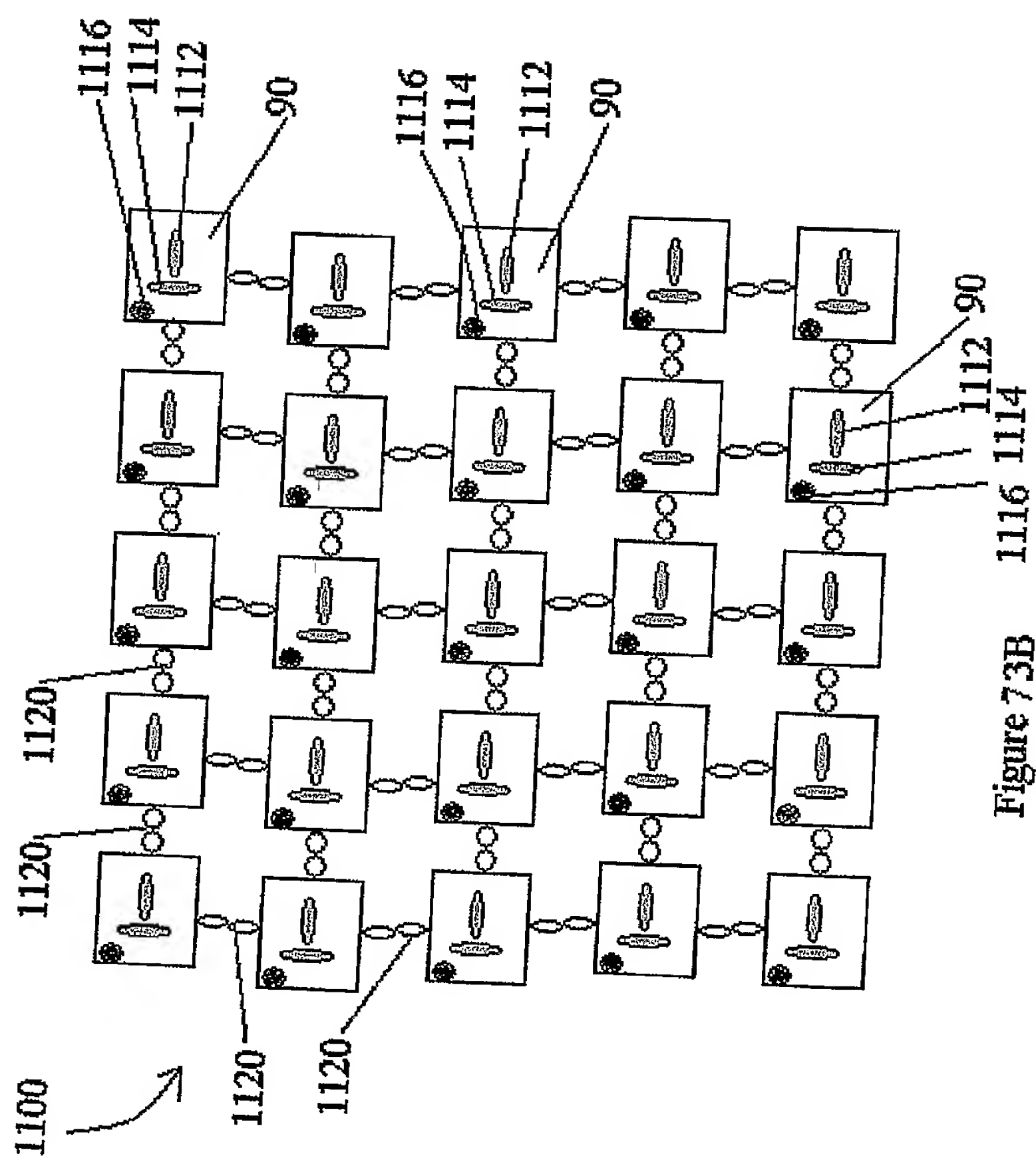


Figure 73B

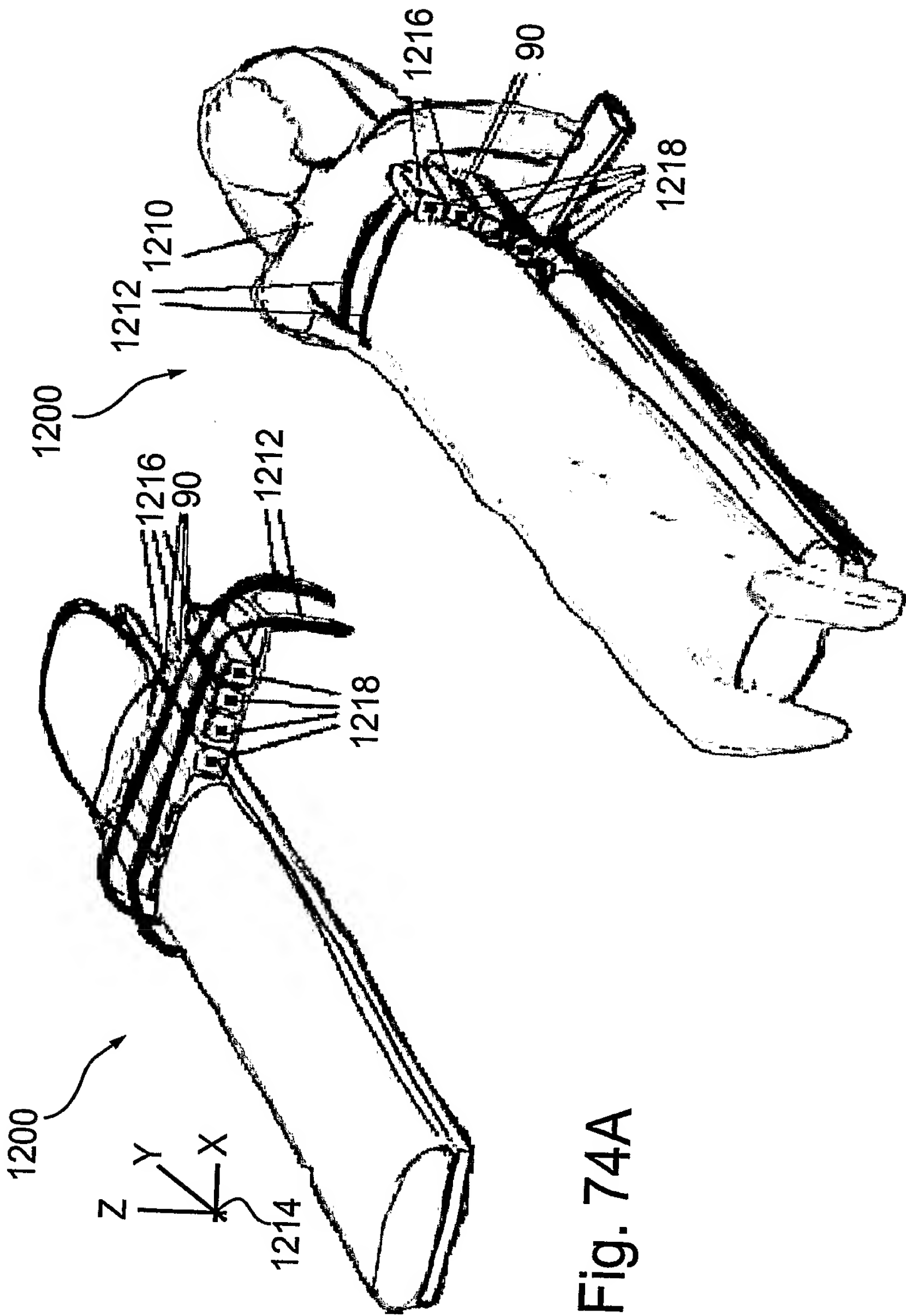


Fig. 74A

Fig. 74B

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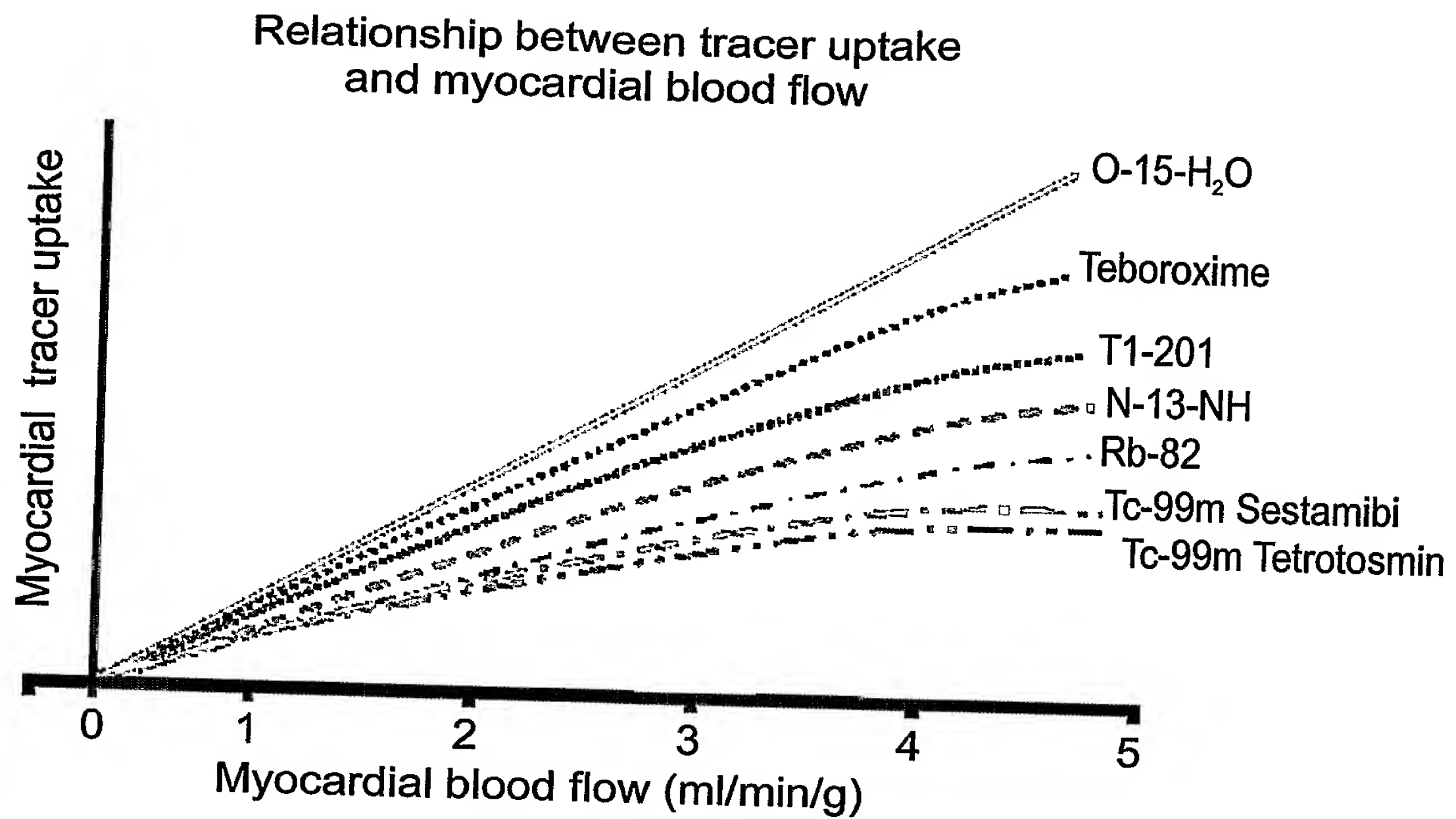


Fig. 75A

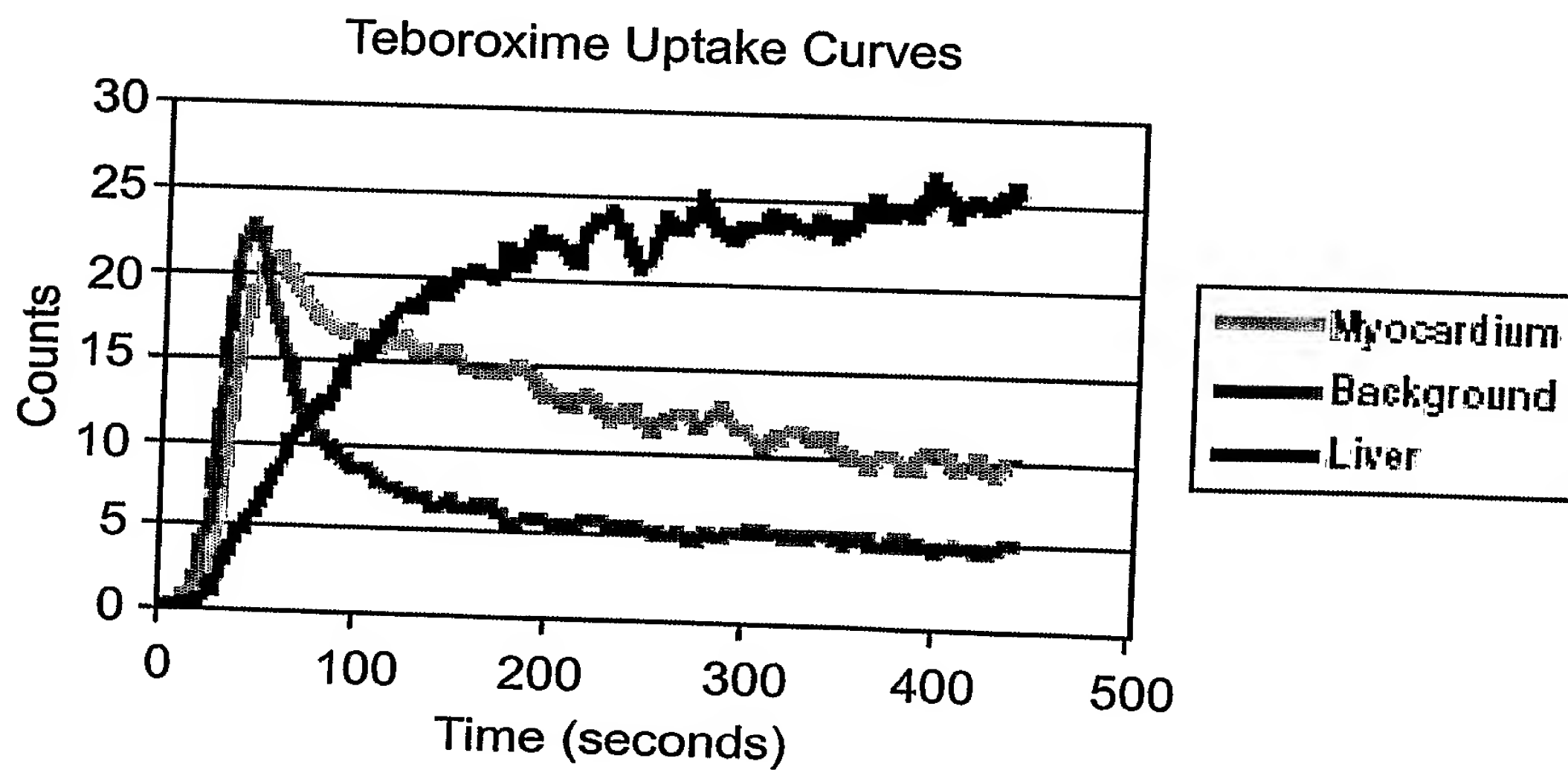


Fig. 75B

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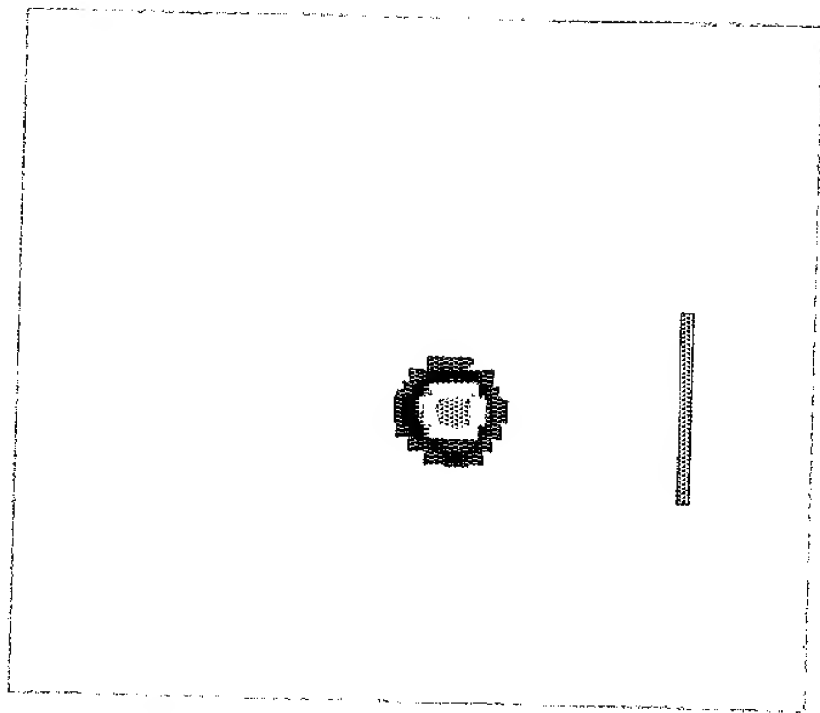


Figure 76A

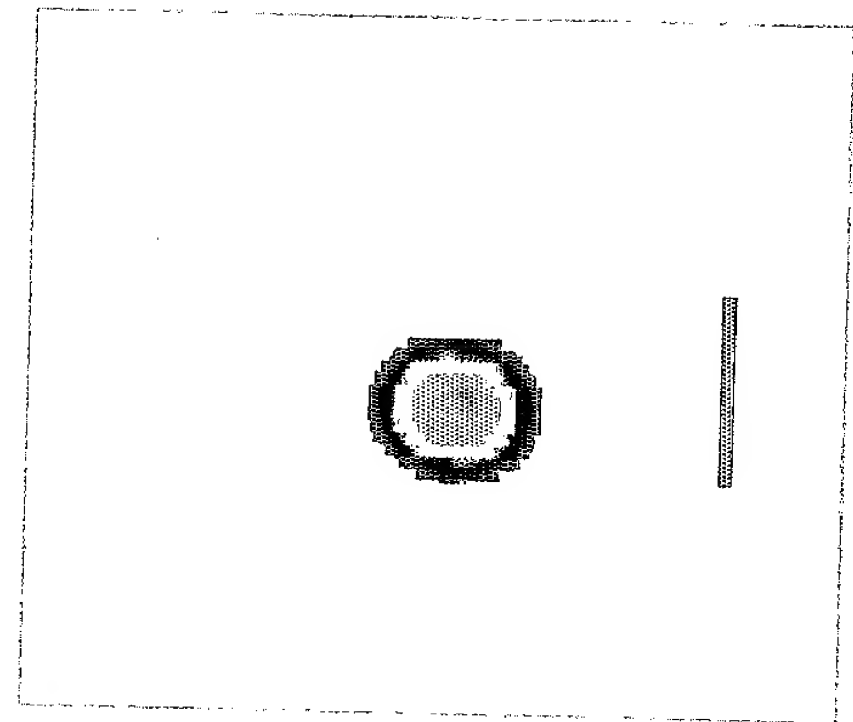


Figure 76B

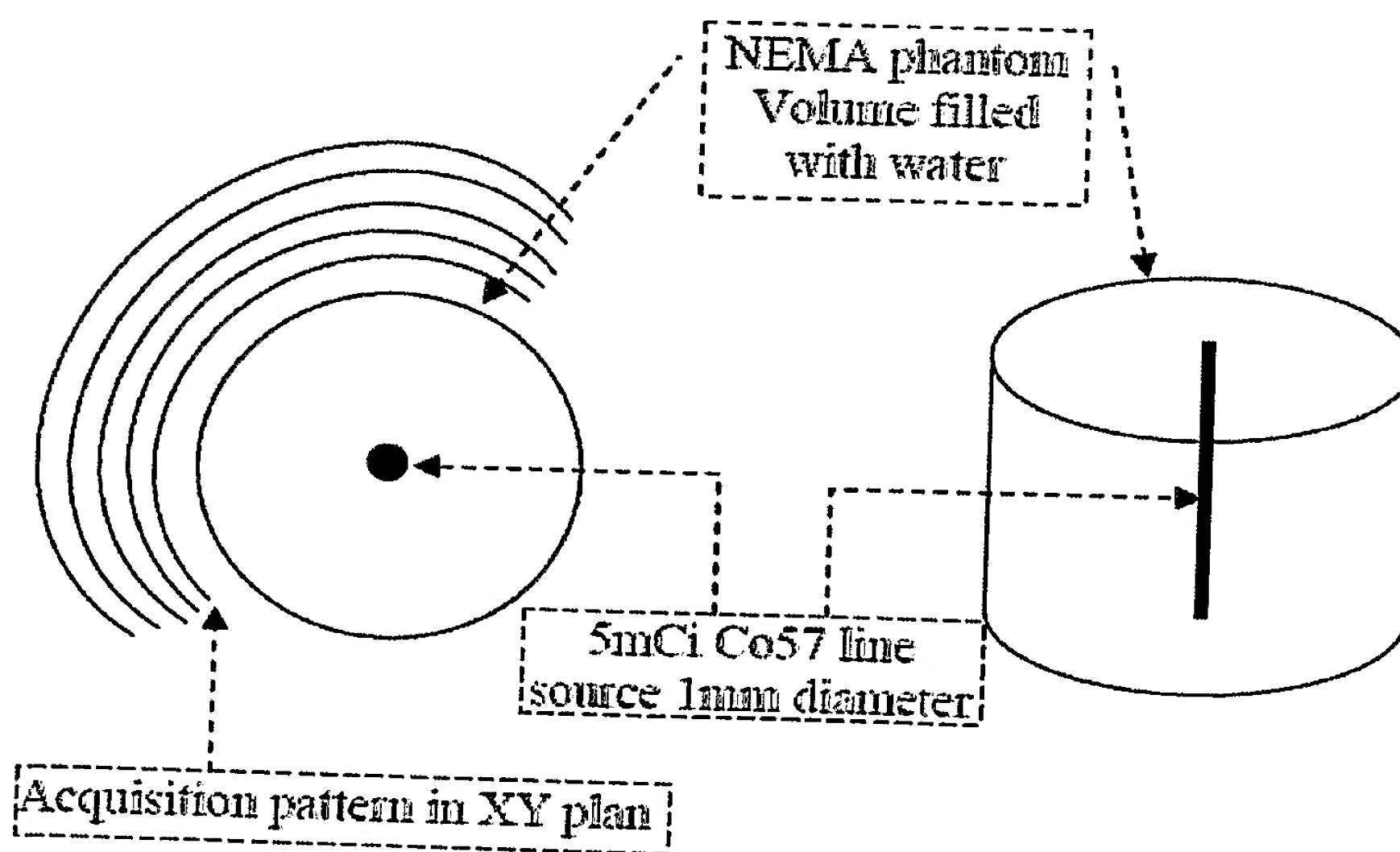


Fig. 76C

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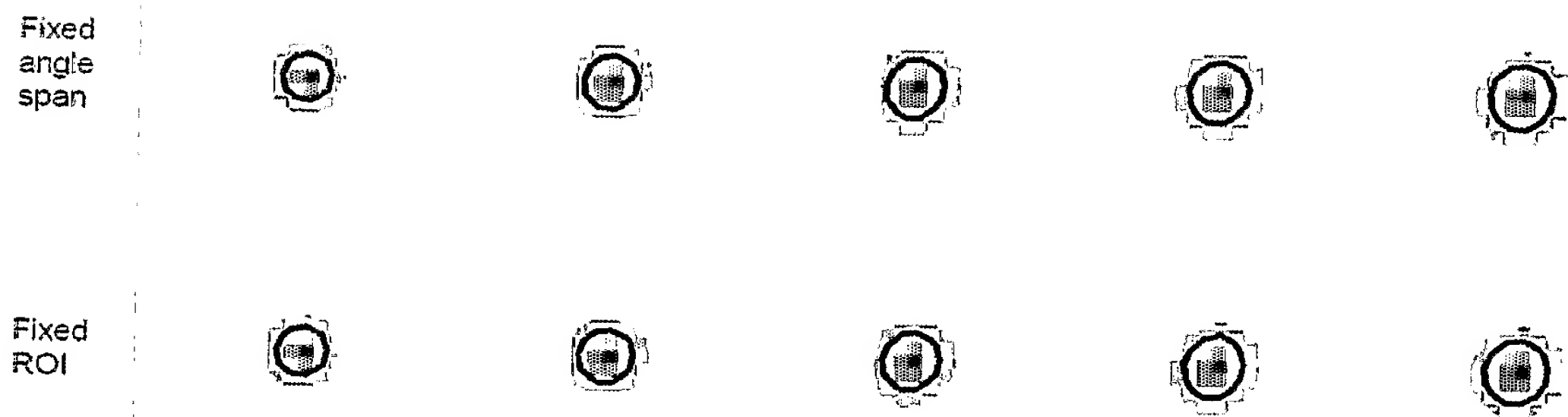
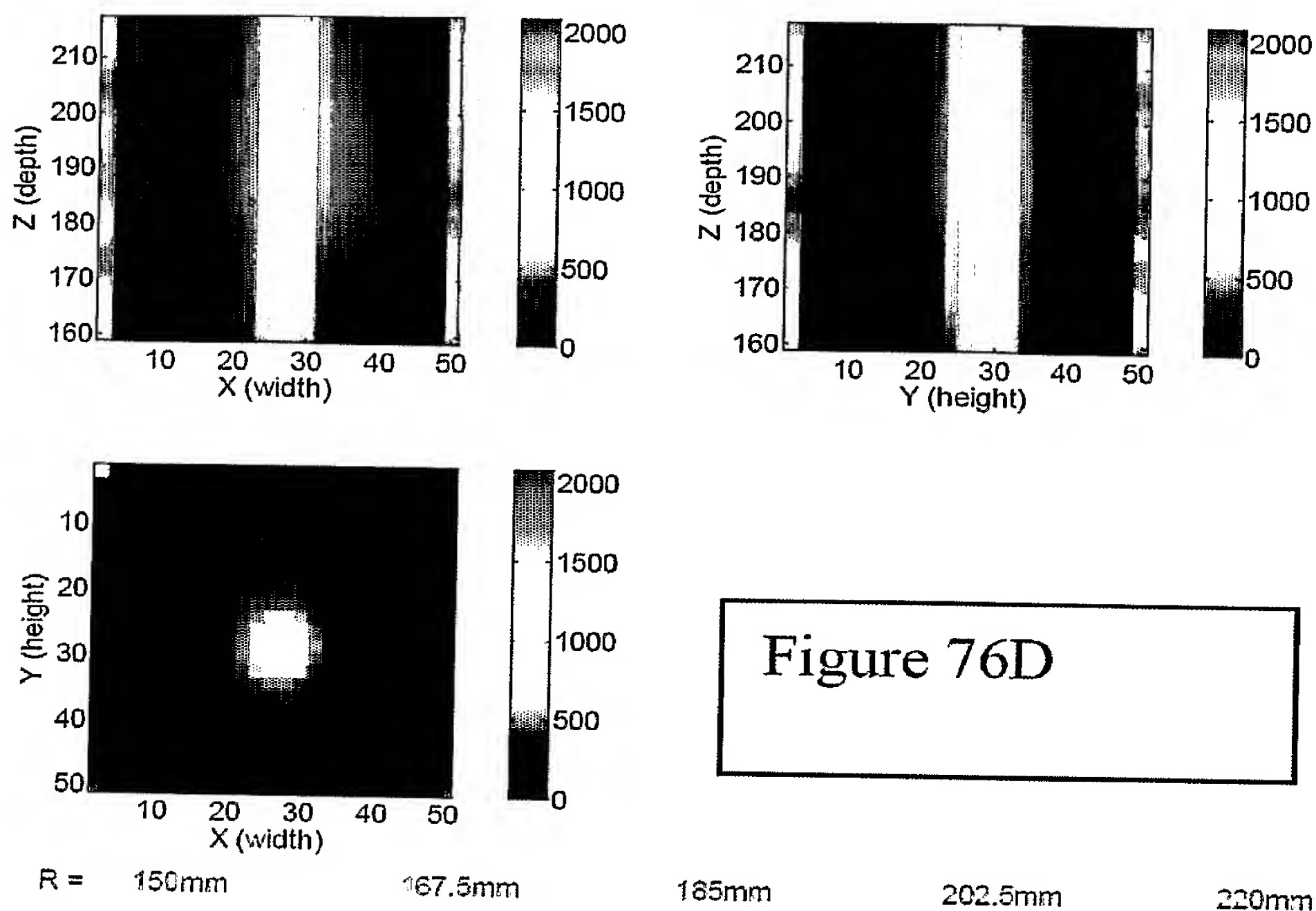


Figure 76E

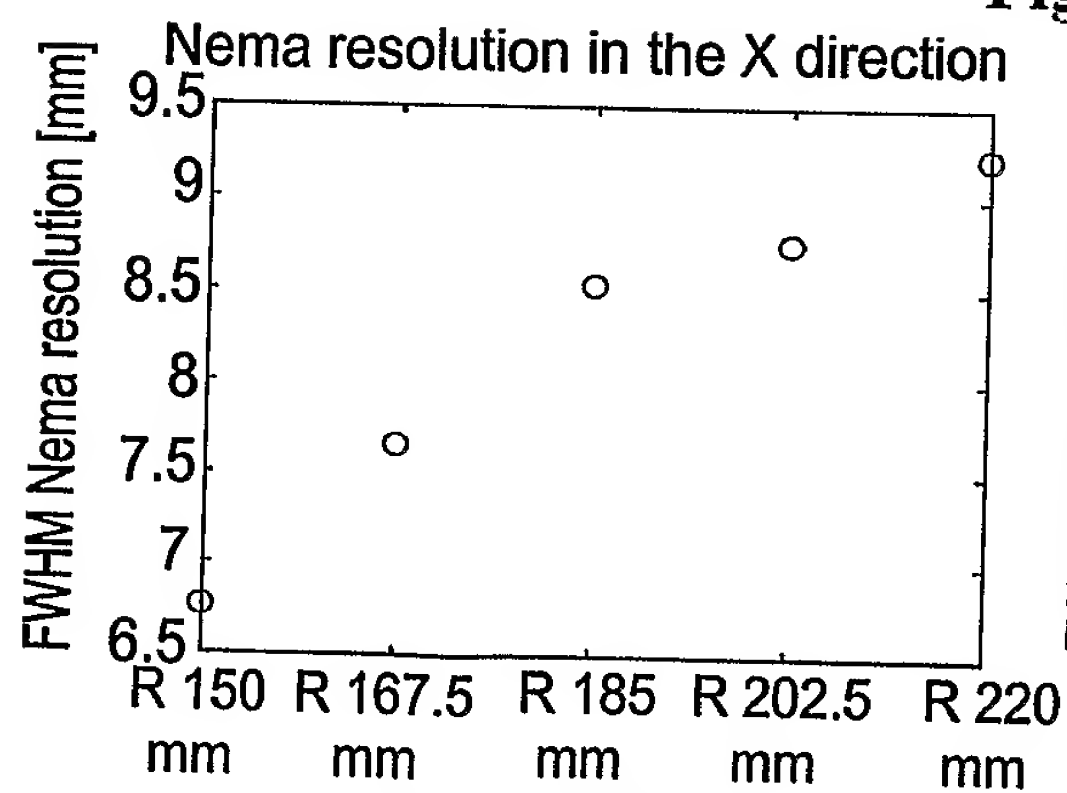


Fig. 76F

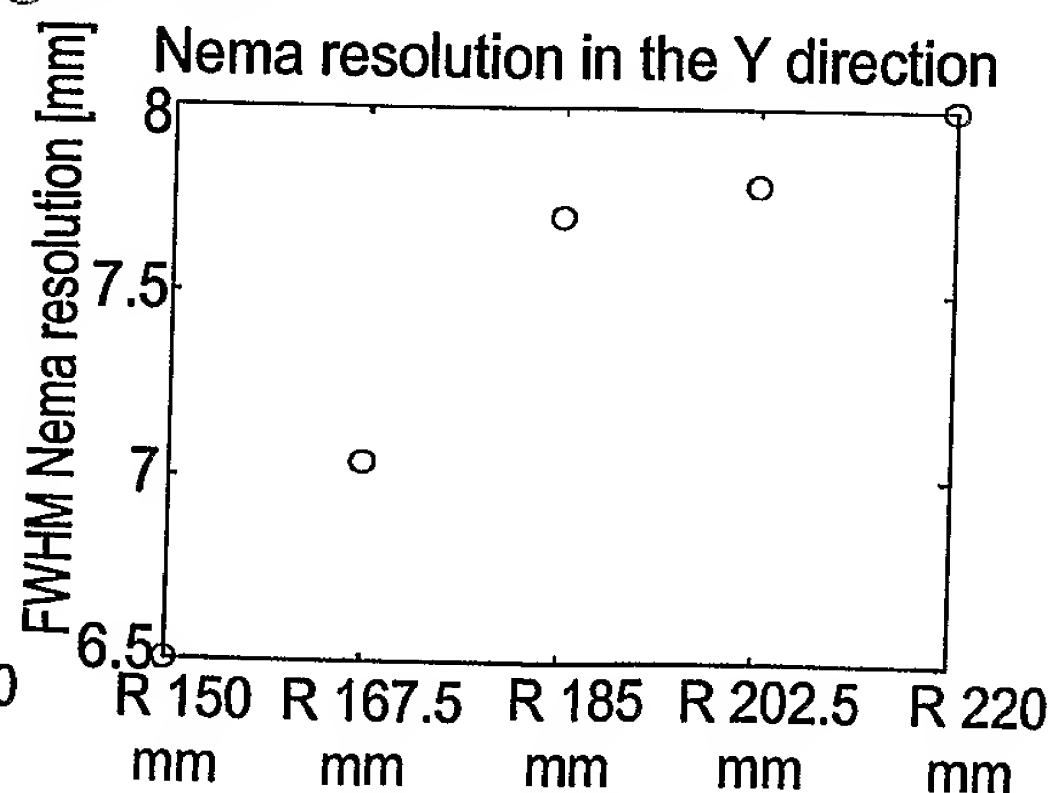


Fig. 76G

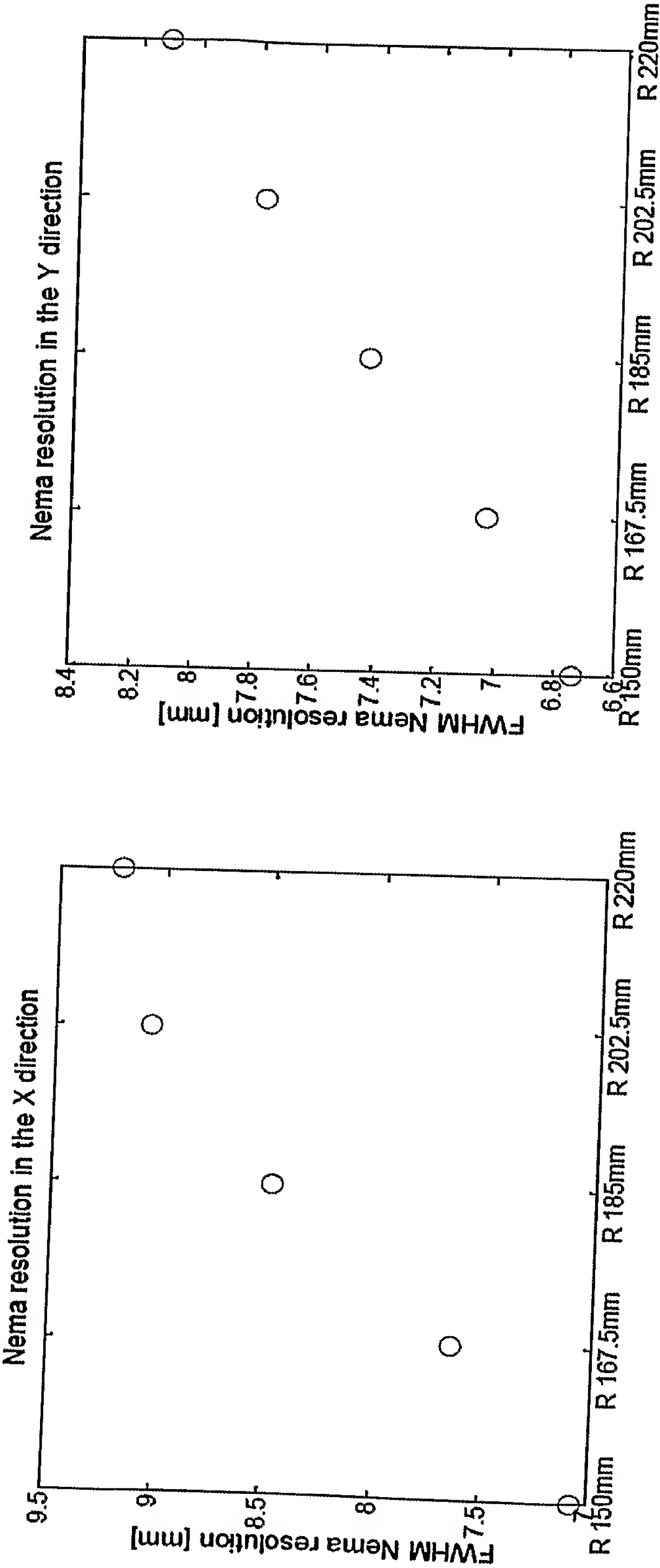
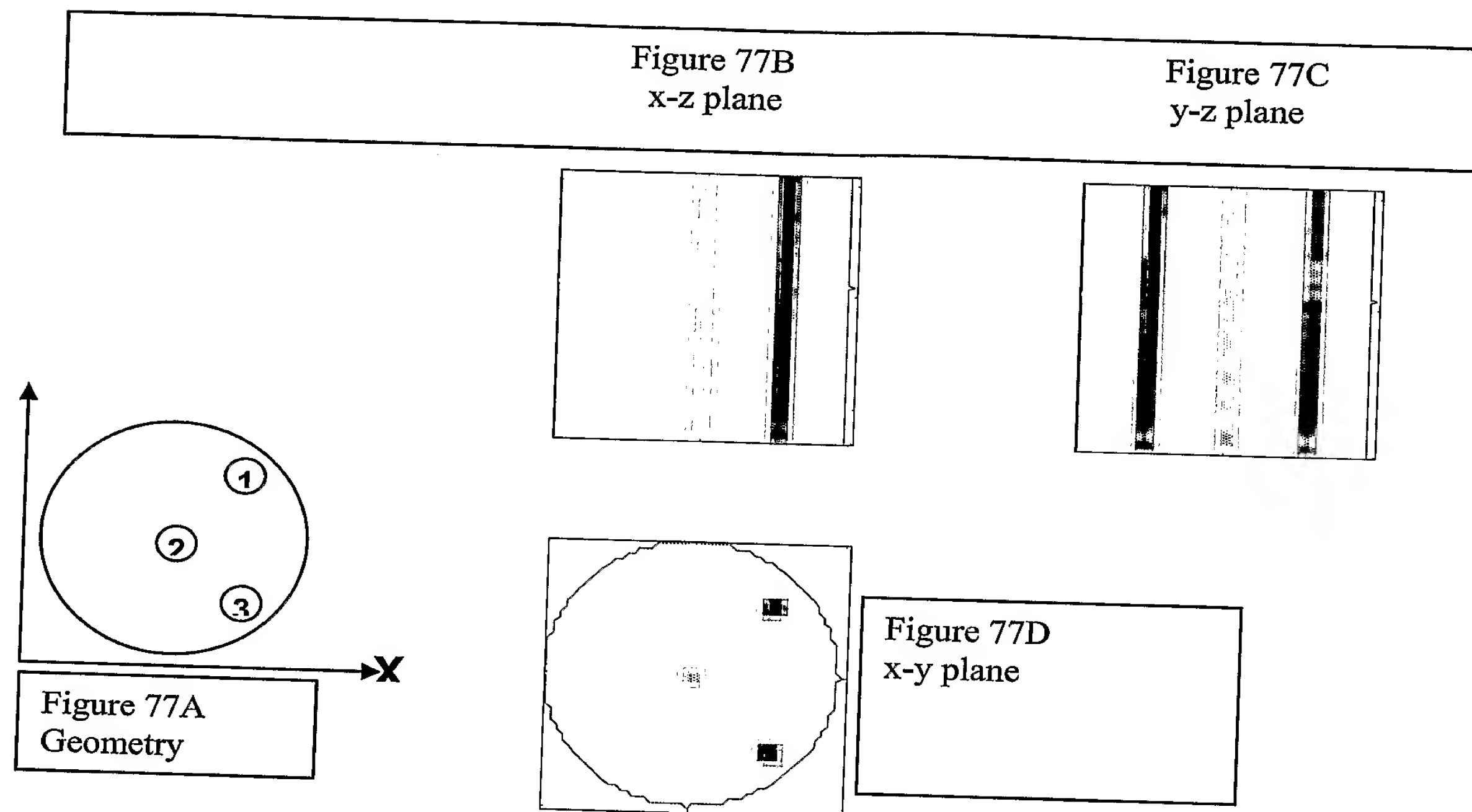


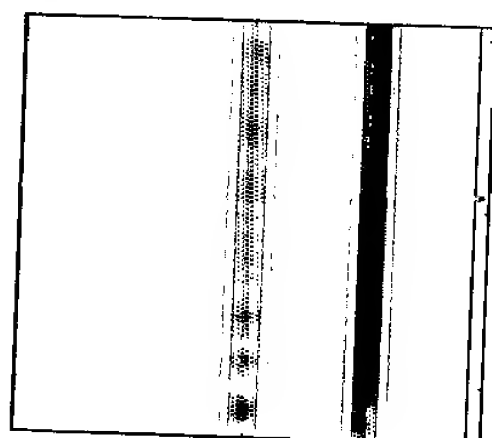
Figure 76H

Figure 76I

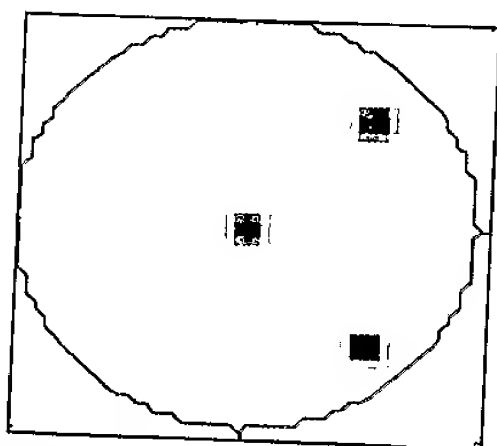
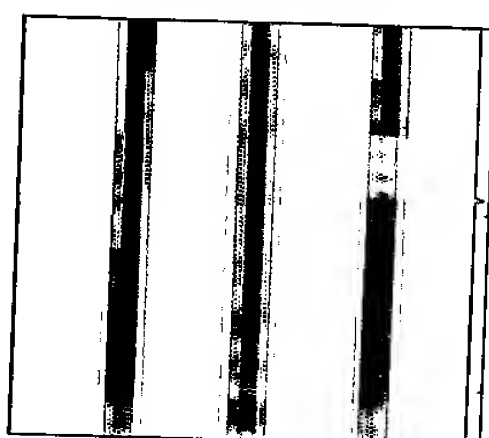
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reconstruction, without attenuation  
correction or smoothing.  
Figures 77E of x-z plane



77F of y-z plane



77G of x-y plane

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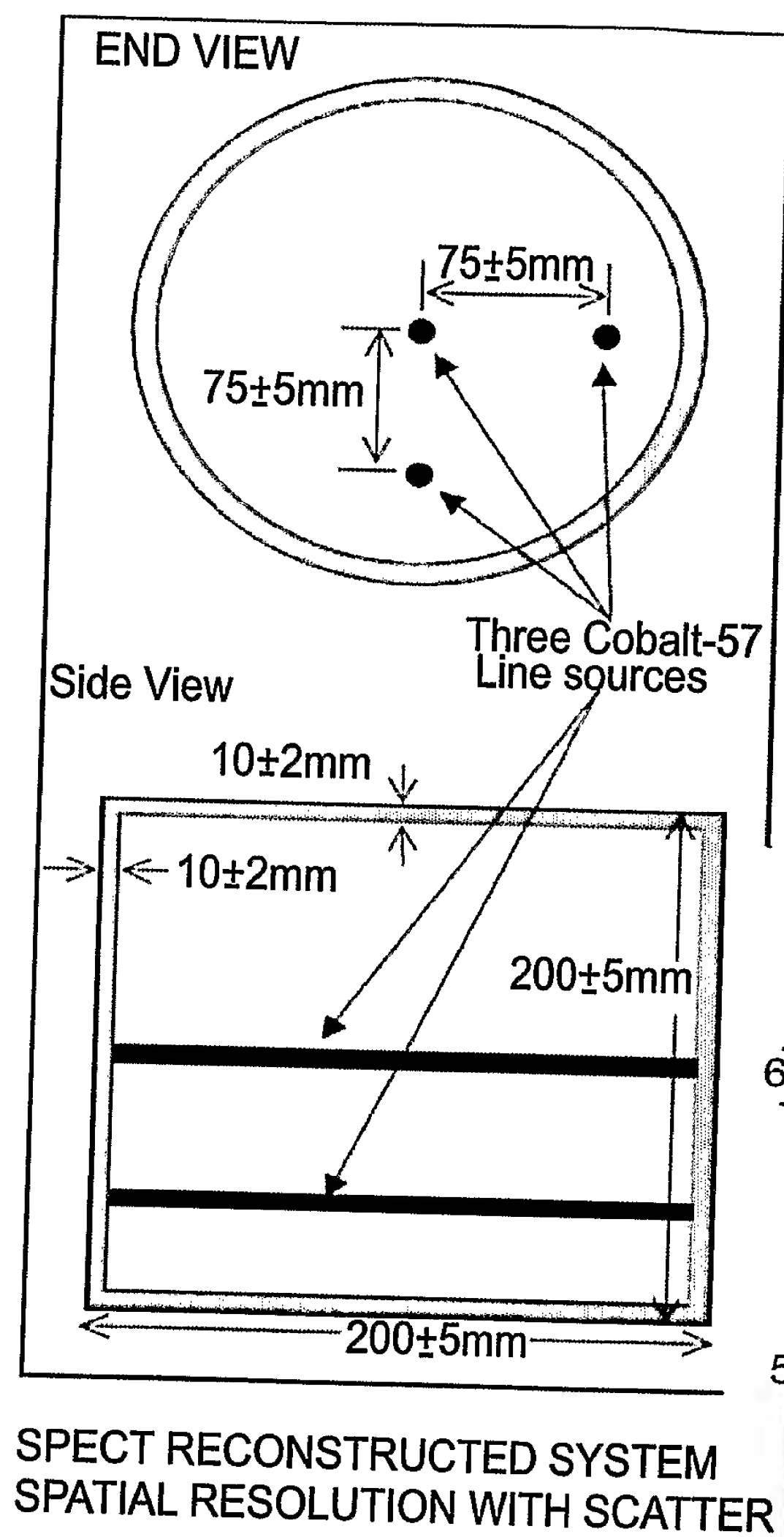


Fig. 78B

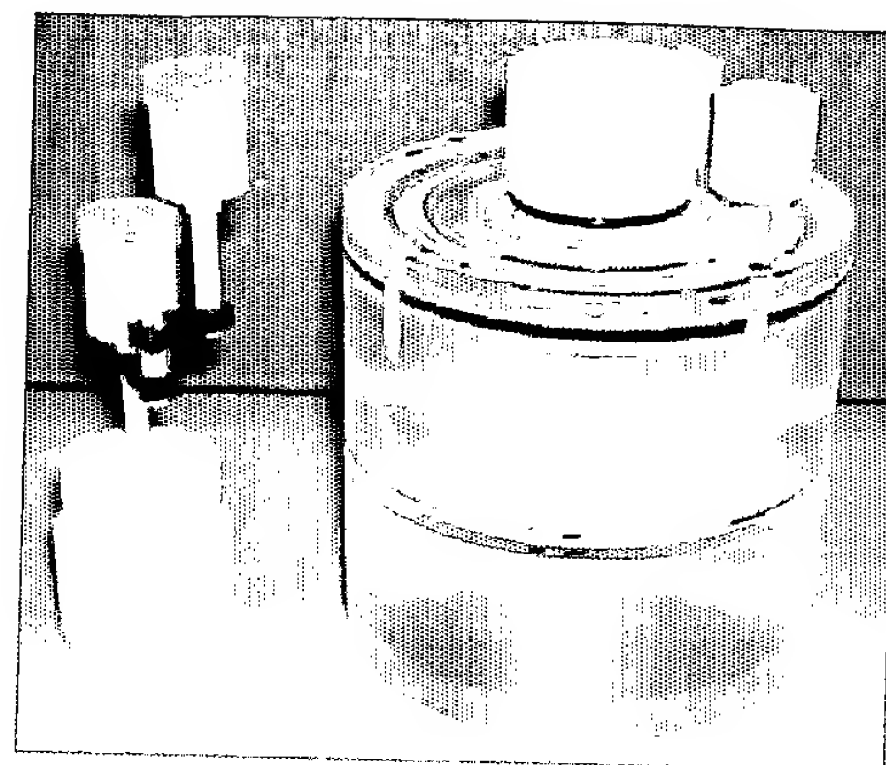
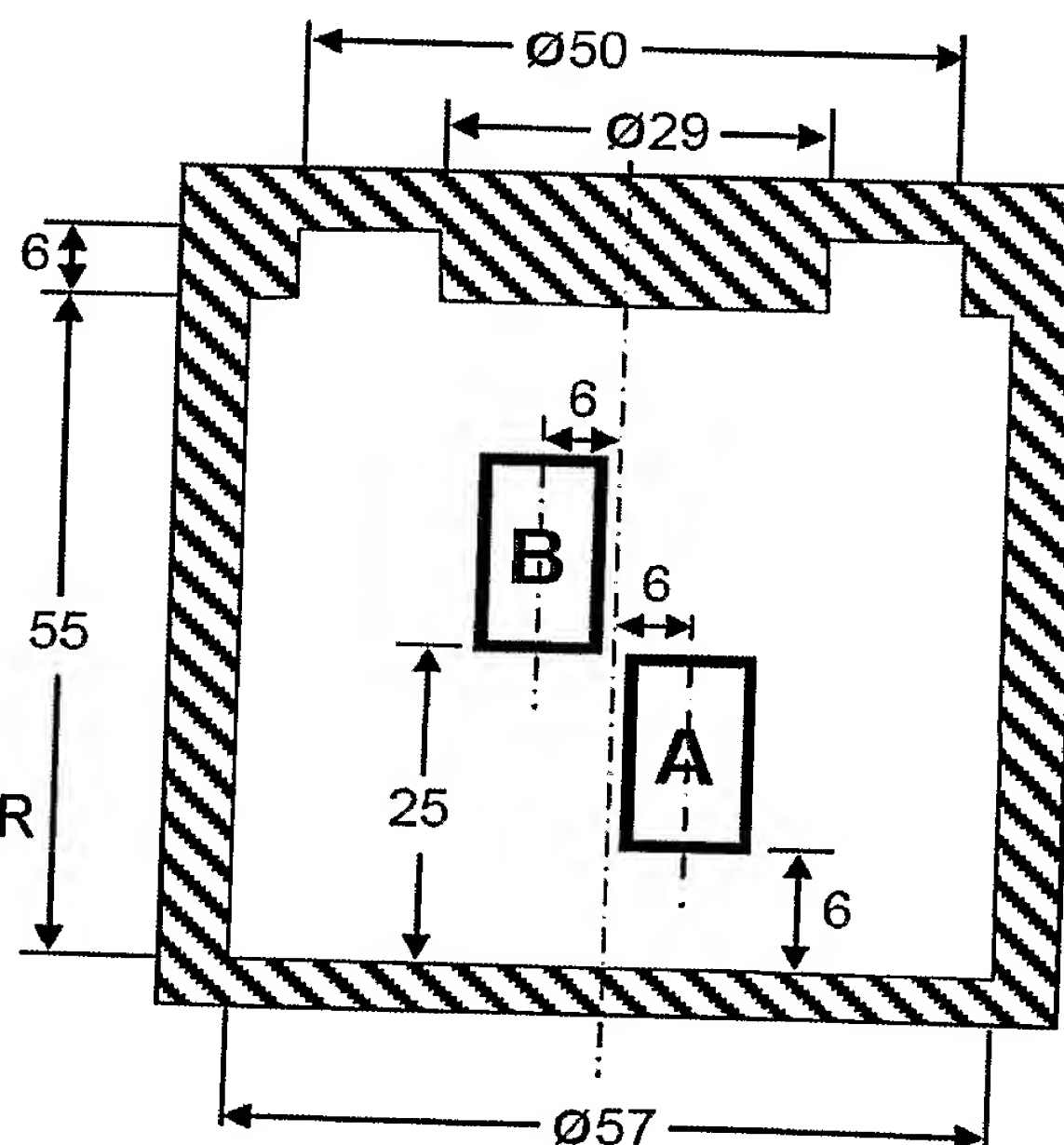


Fig. 78A



A,B: Ø10 h=15  
 Target volume: 1.17cc  
 Background volume: 158cc

Fig. 78C



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Figure 79A of x-z plane

Figure 79B of y-z plane

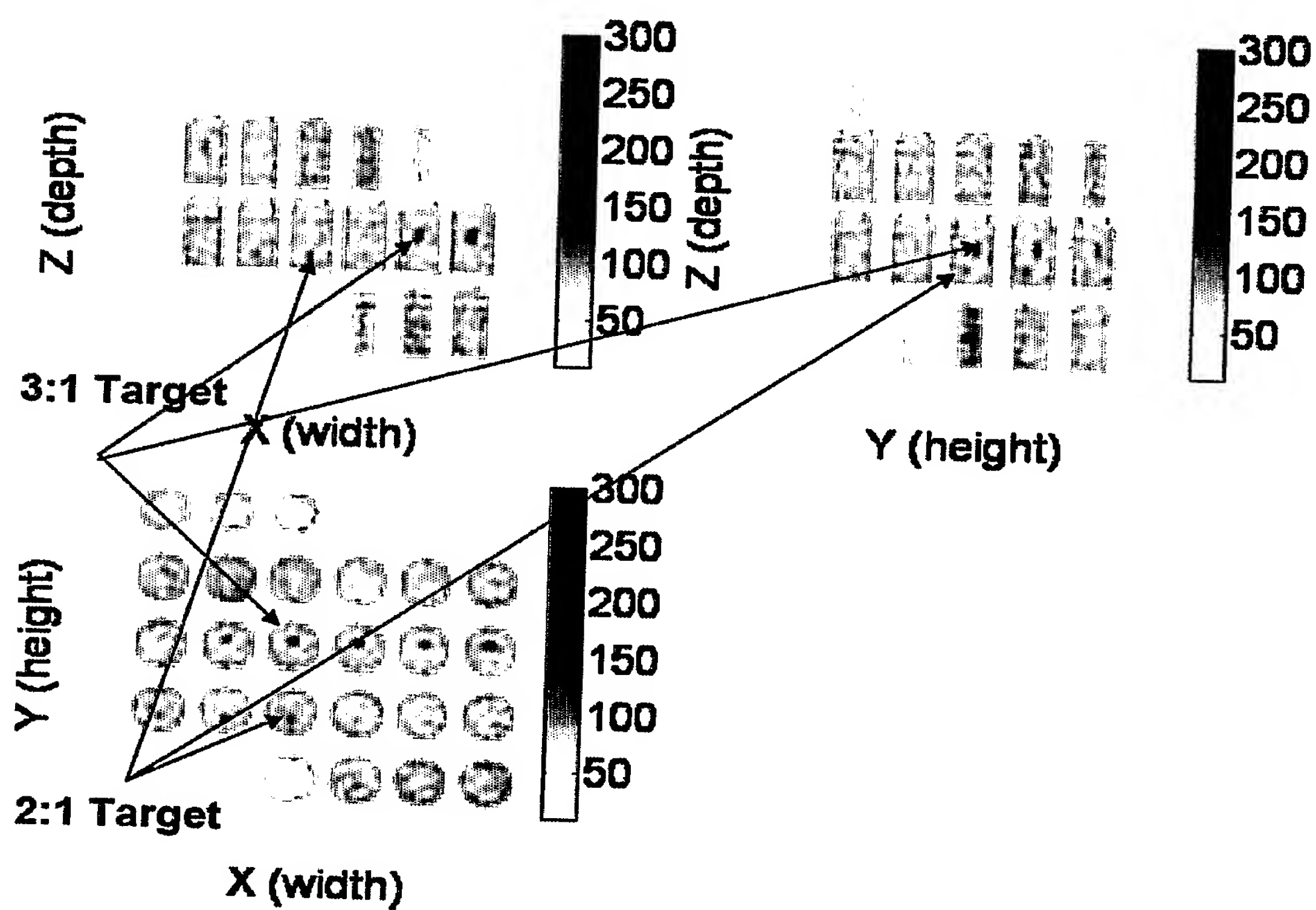


Figure 79C of x-y plane

Conventional Camera

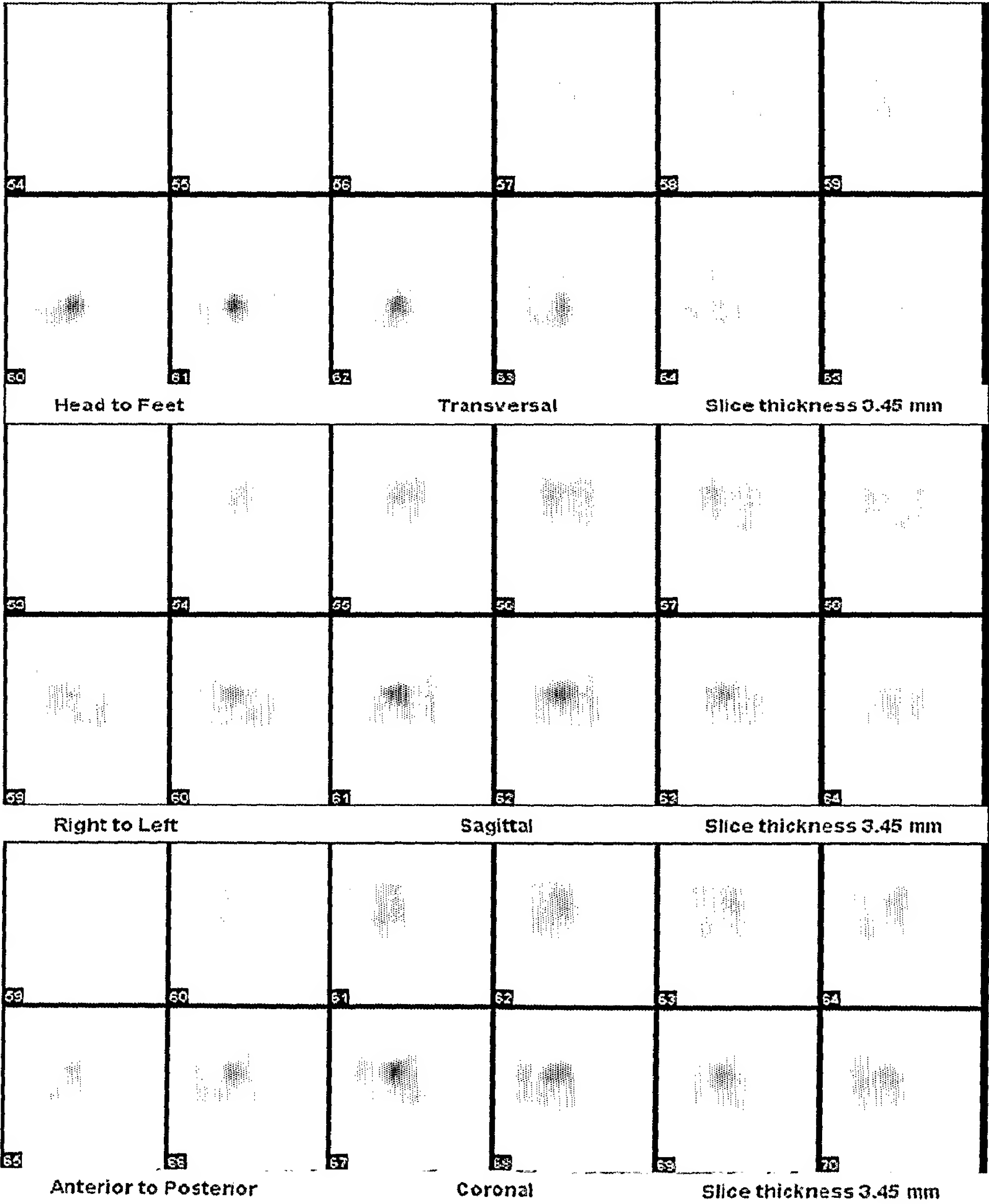
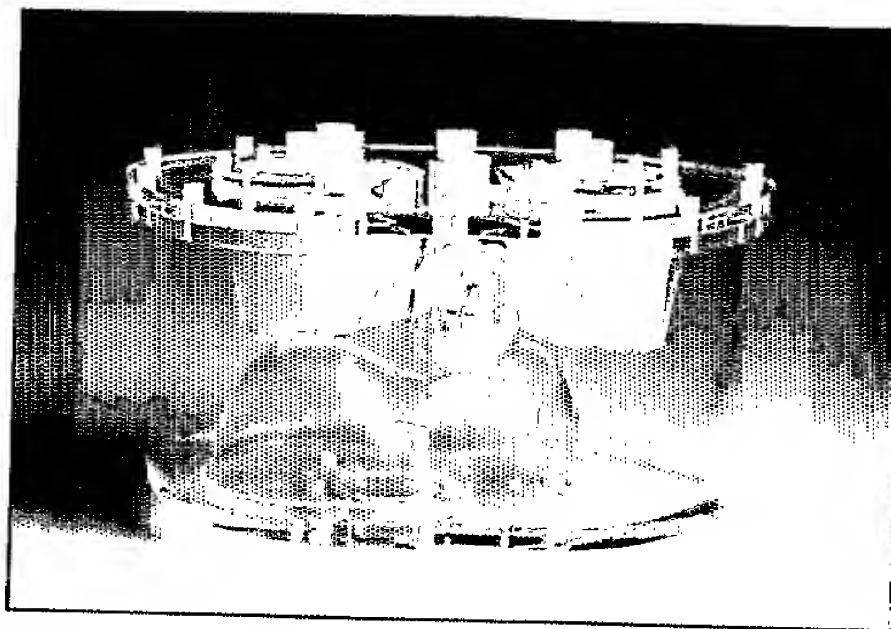


Figure 79D

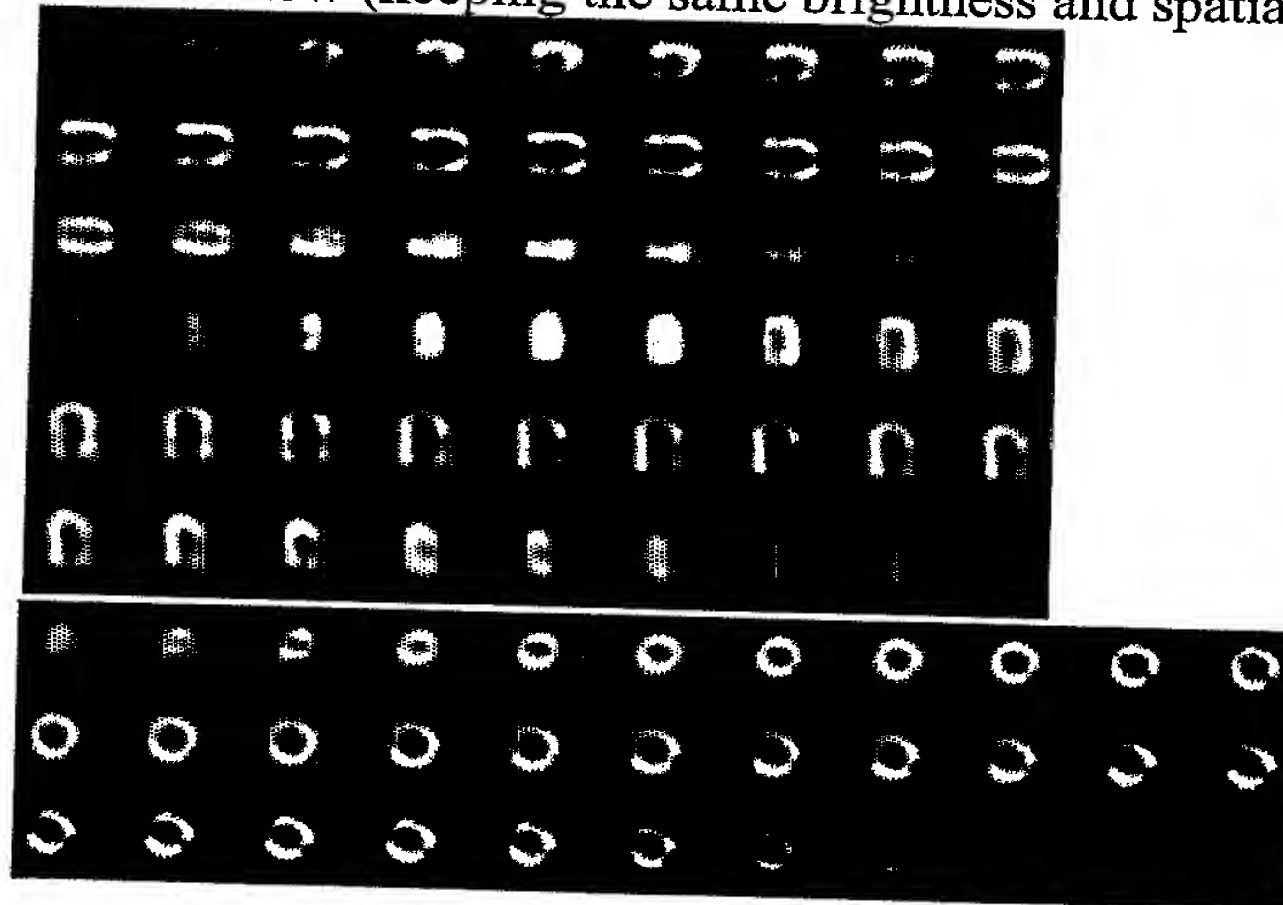
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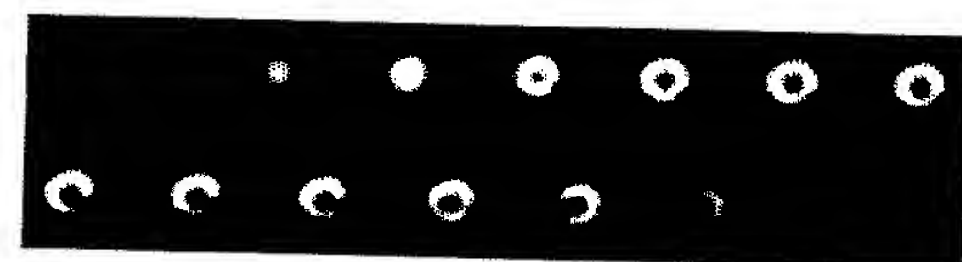
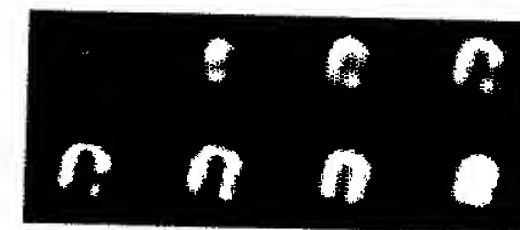
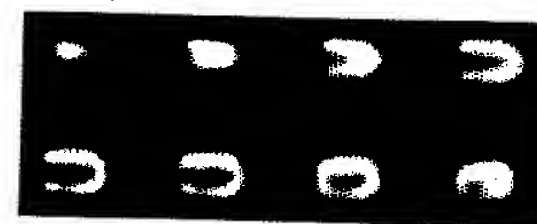
Anthropomorphic Torso Phantom  
Model ECT/TOR/P  
Produced by Data Spectrum  
Corporation, USA

Figure 80A

The resulting reconstructions as compared to that performed by the conventional camera are shown below (keeping the same brightness and spatial scale):



**Figure 80B**  
probe of the present invention  
Net Acquisition time = 1.25min



**Figure 80C**  
Conventional Camera  
Net Acquisition time= 12.5min

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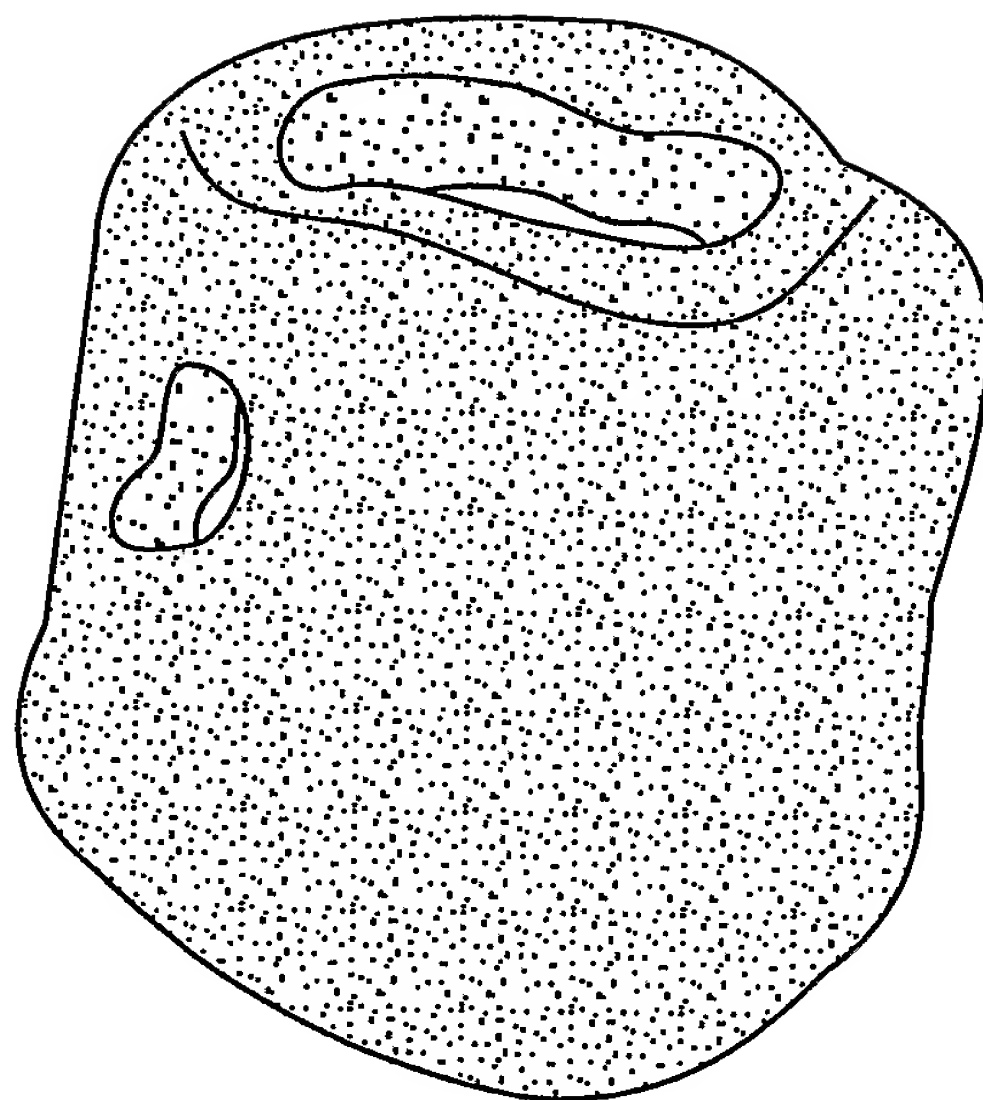


Fig. 80D

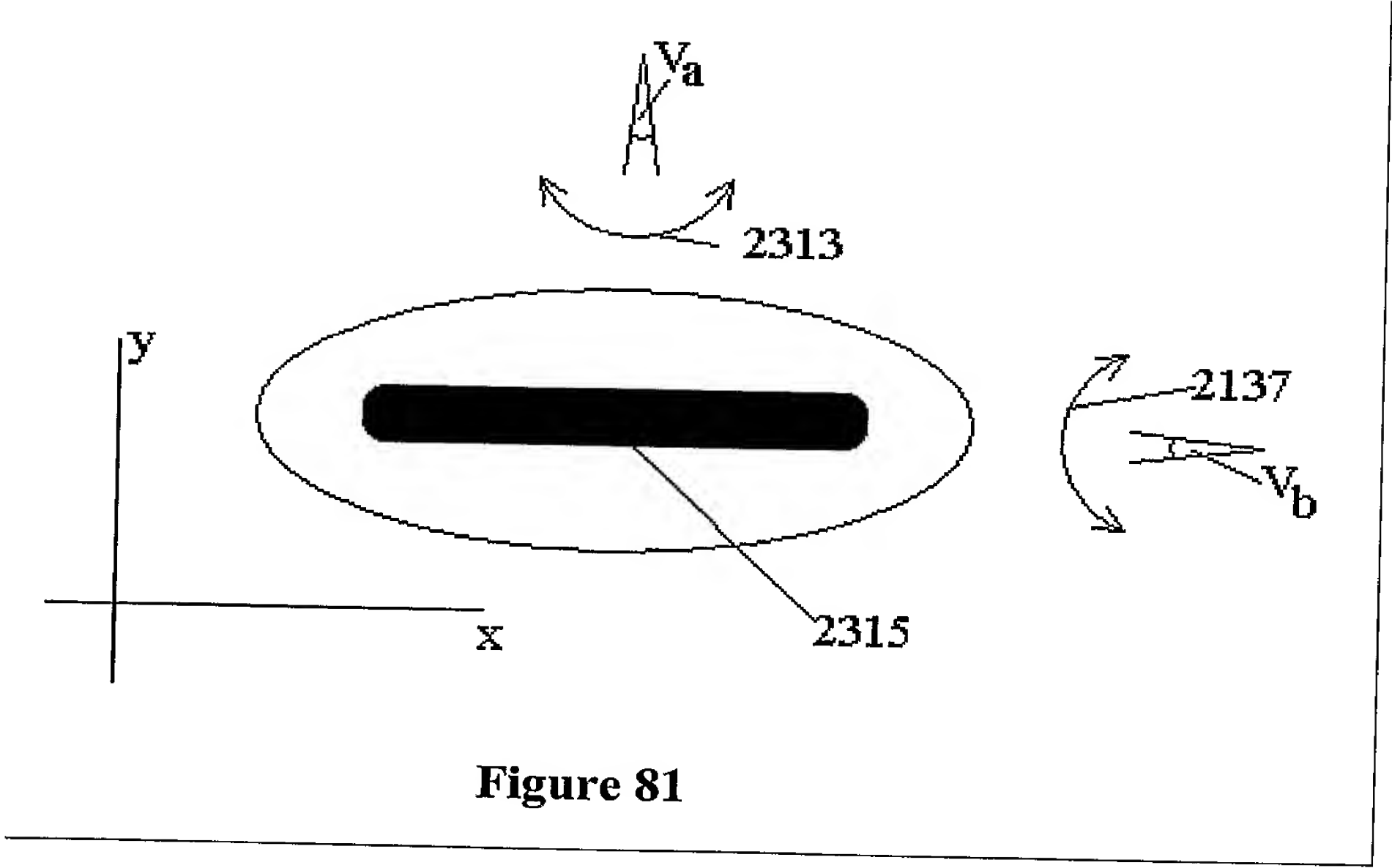
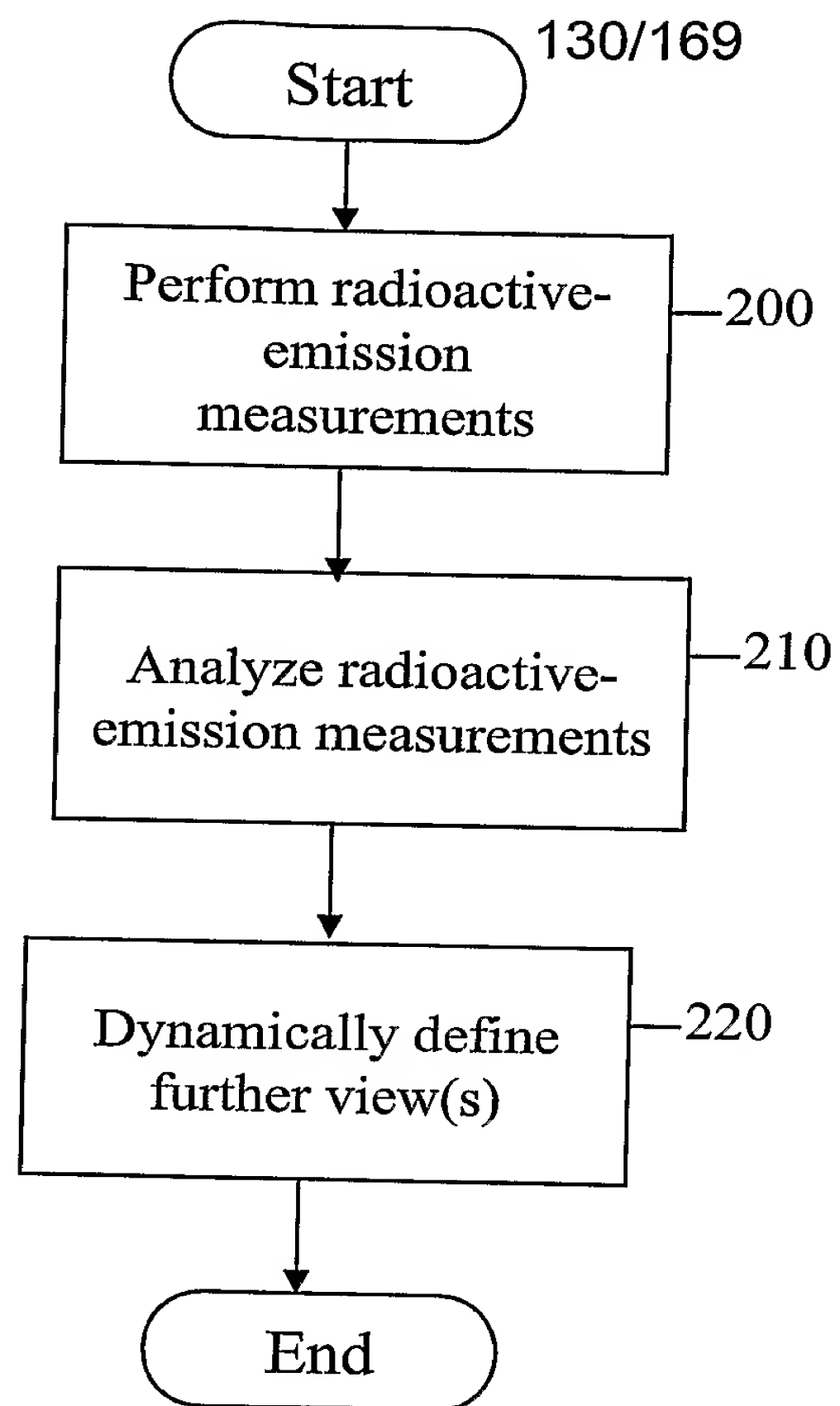


Figure 81

**Figure 82**

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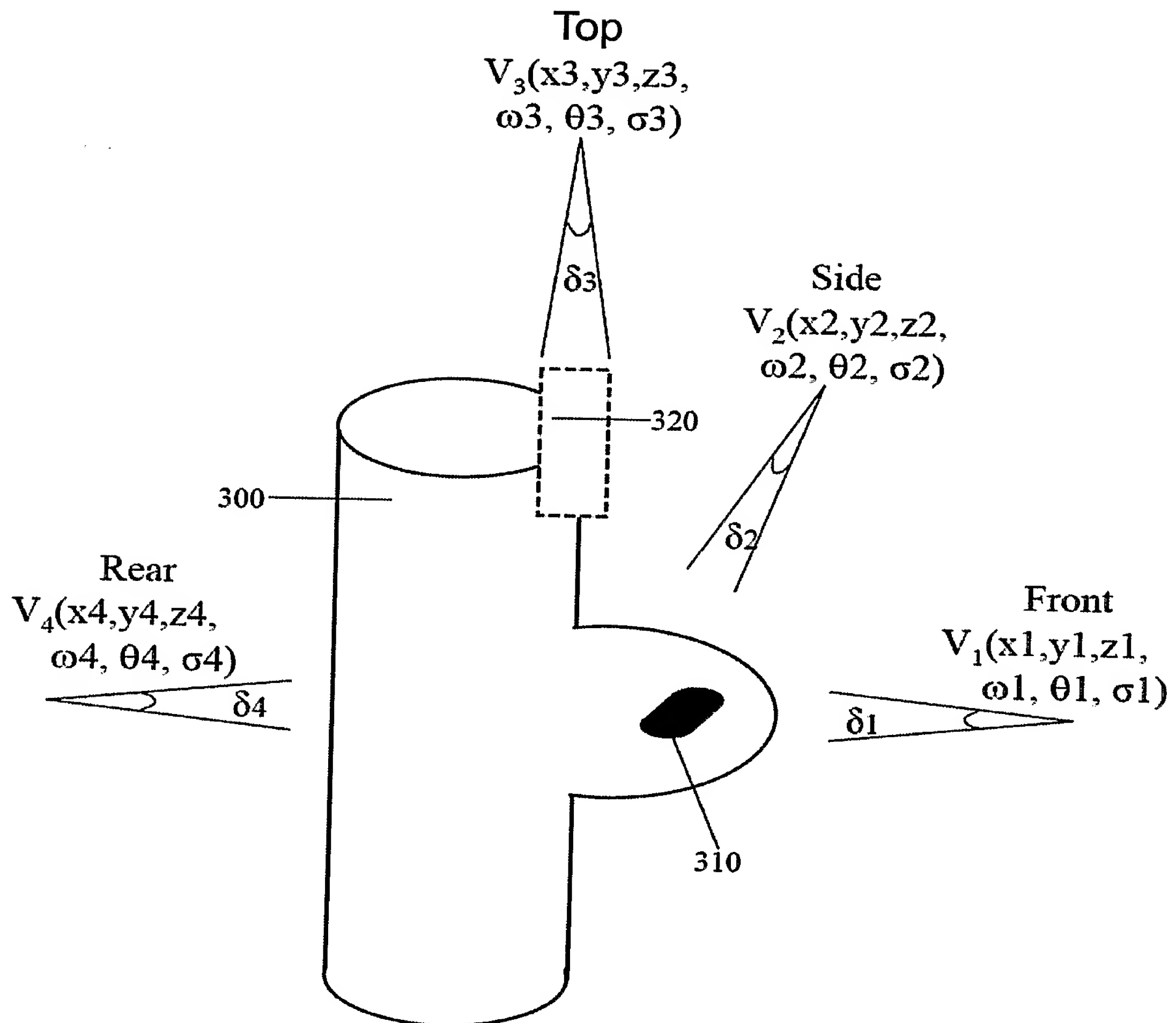


Fig. 83

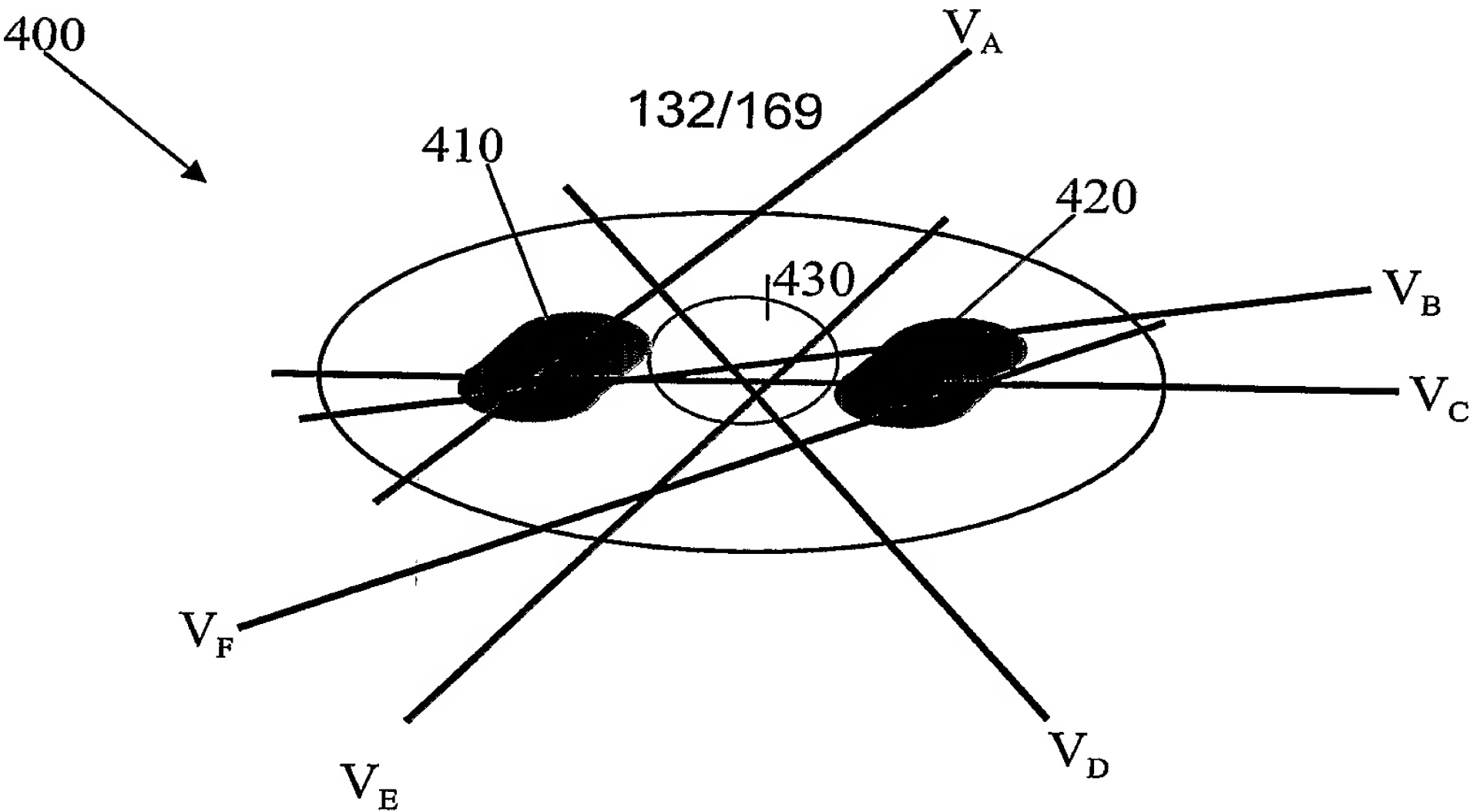


Figure 84a

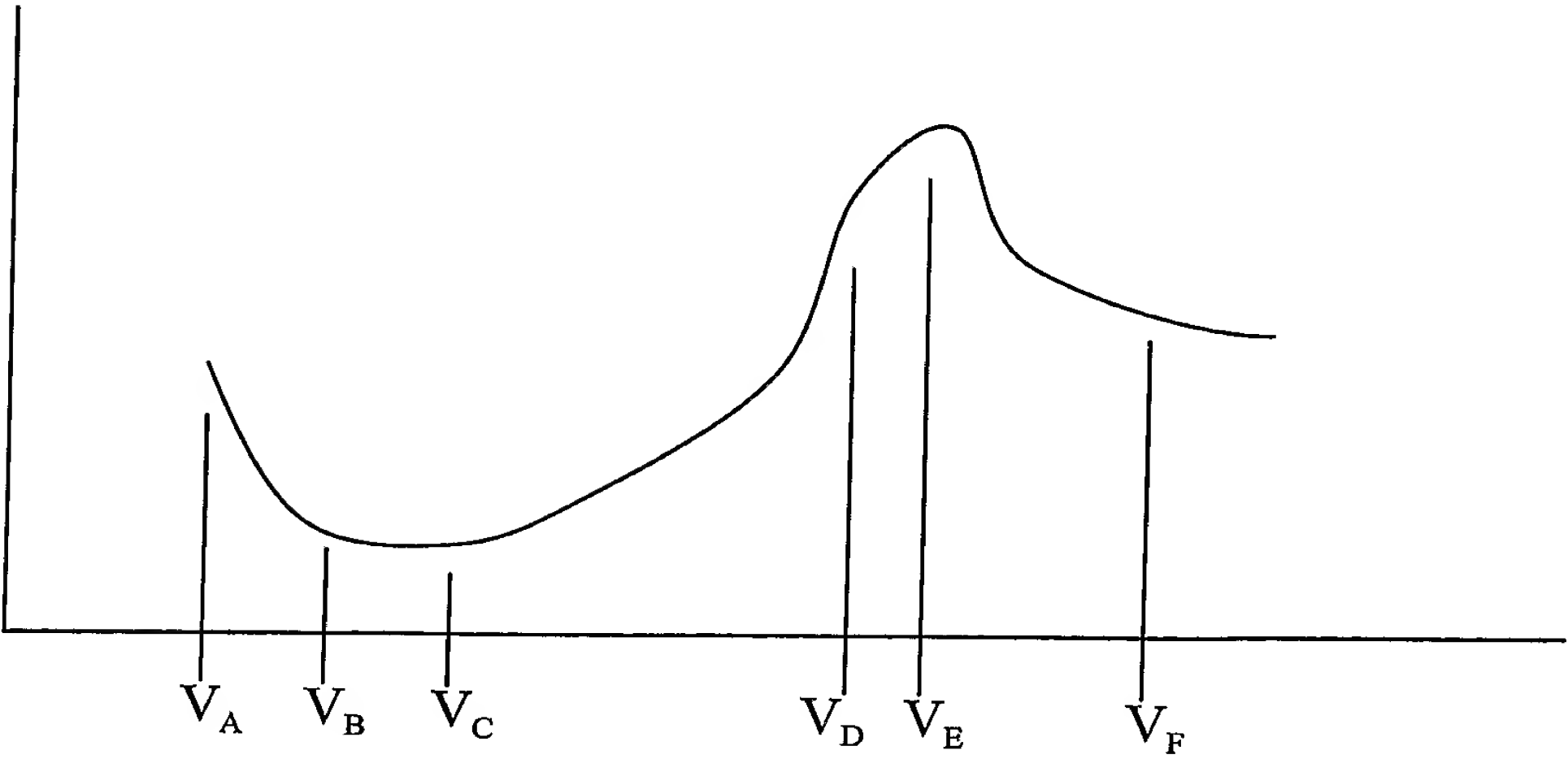
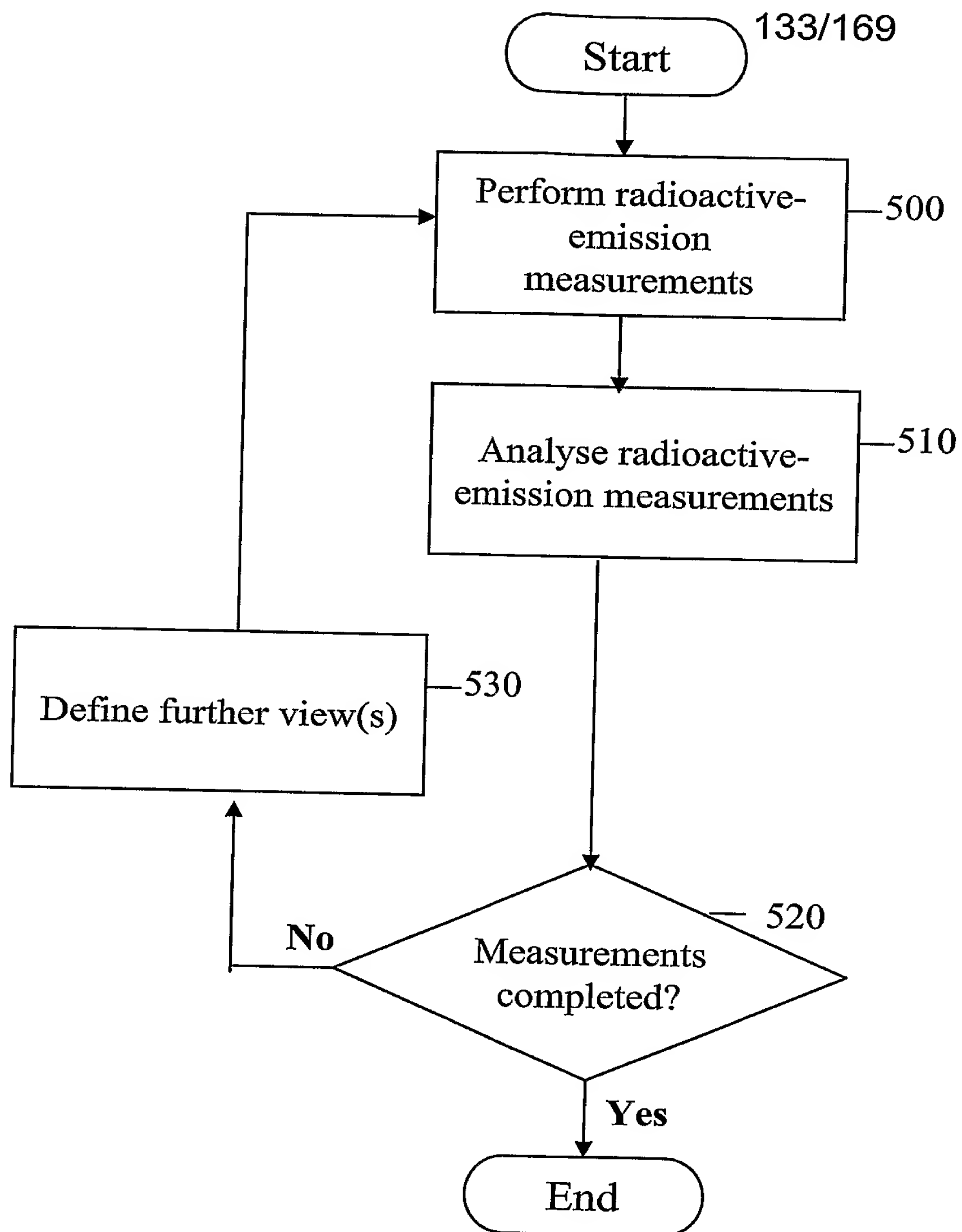


Figure 84b



**Figure 85a**

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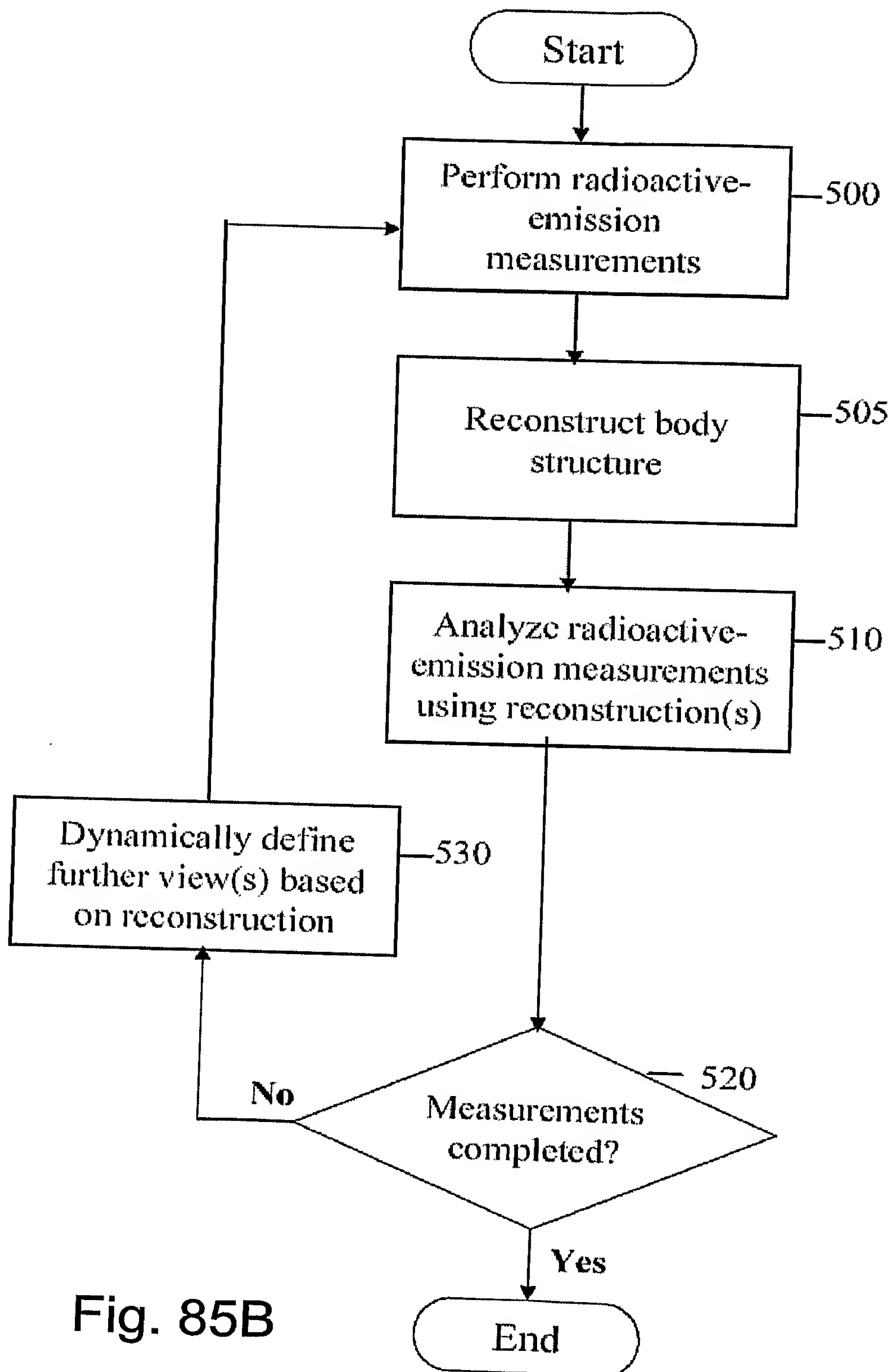
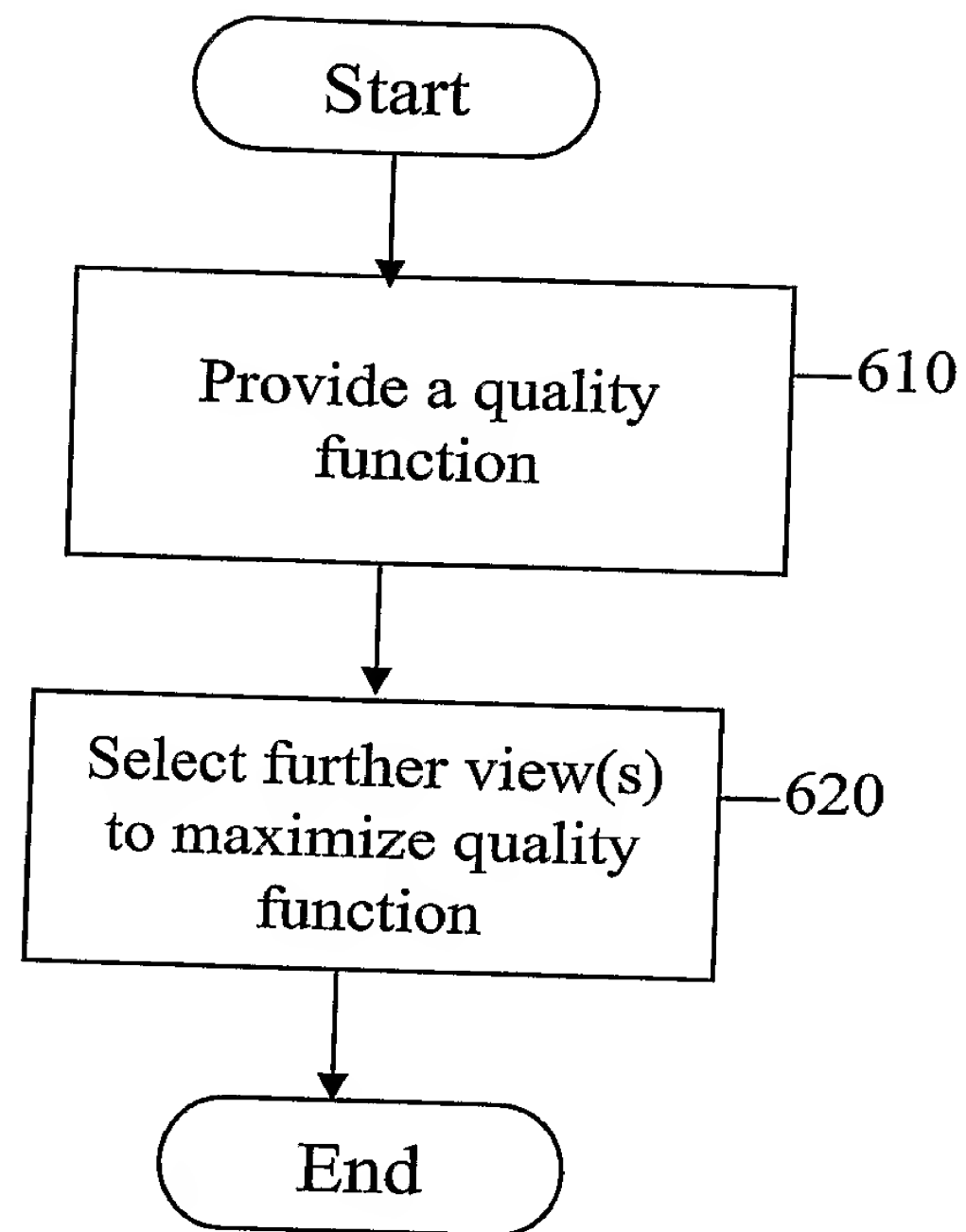
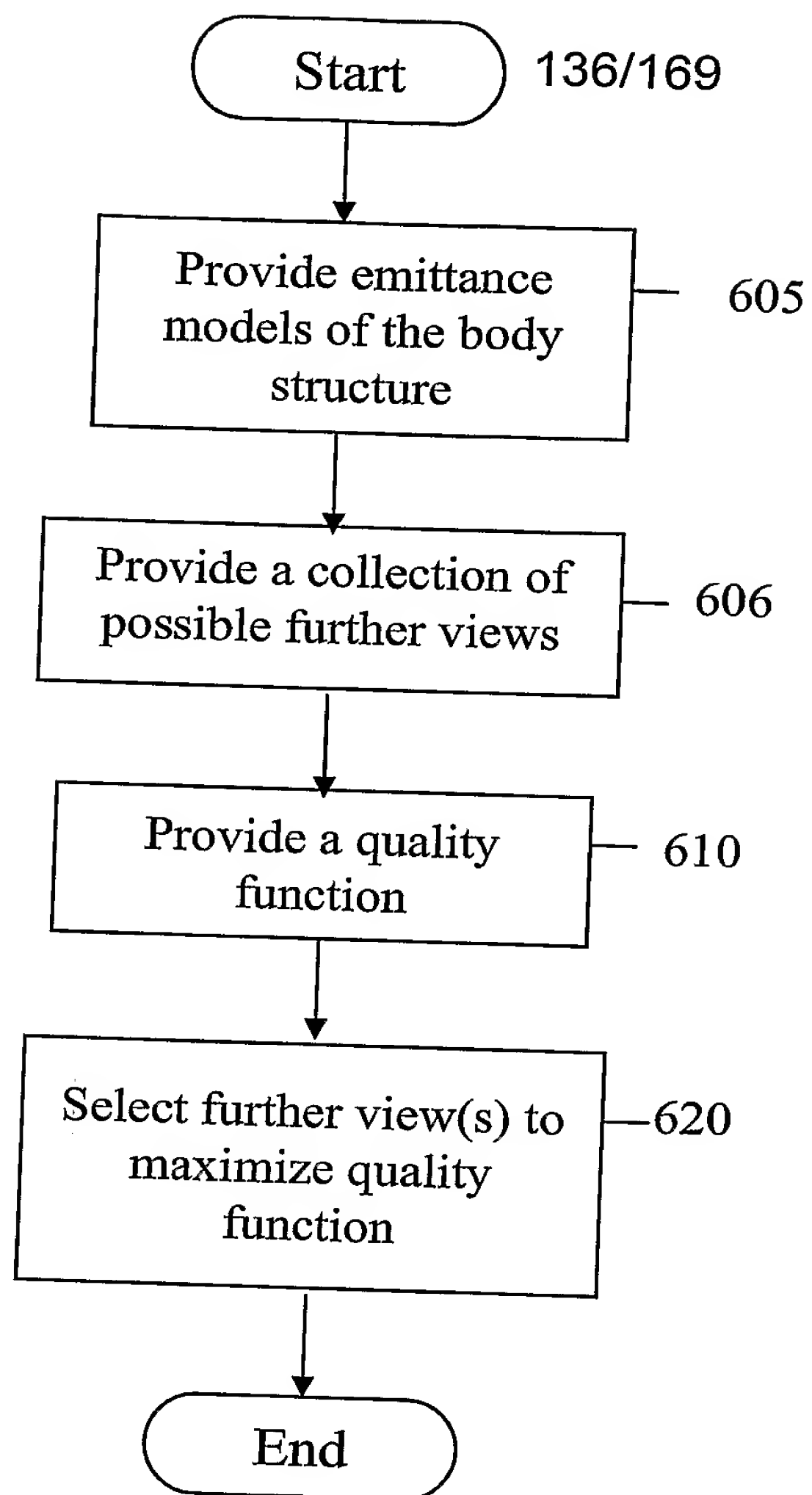


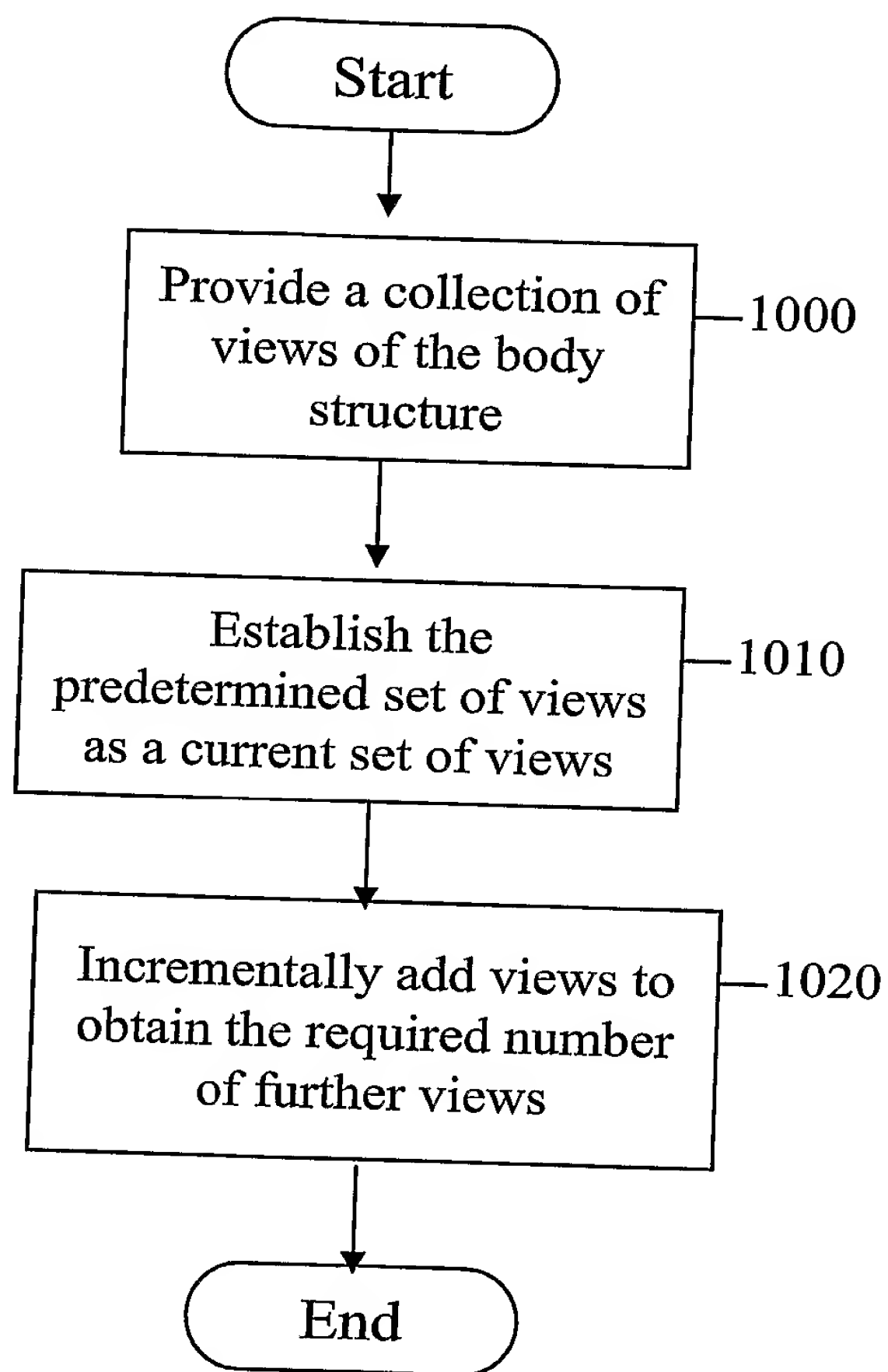
Fig. 85B

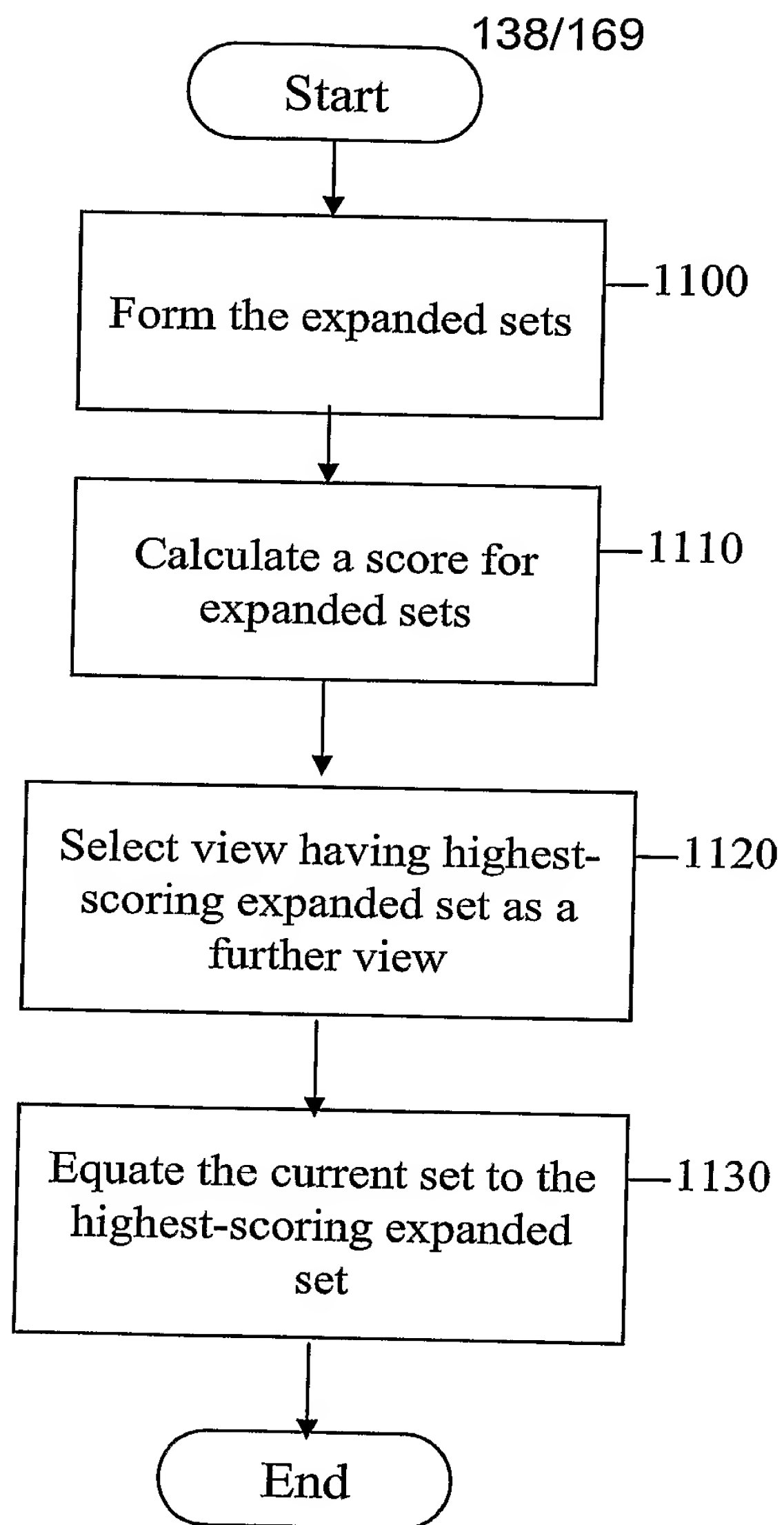
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**Figure 86a**

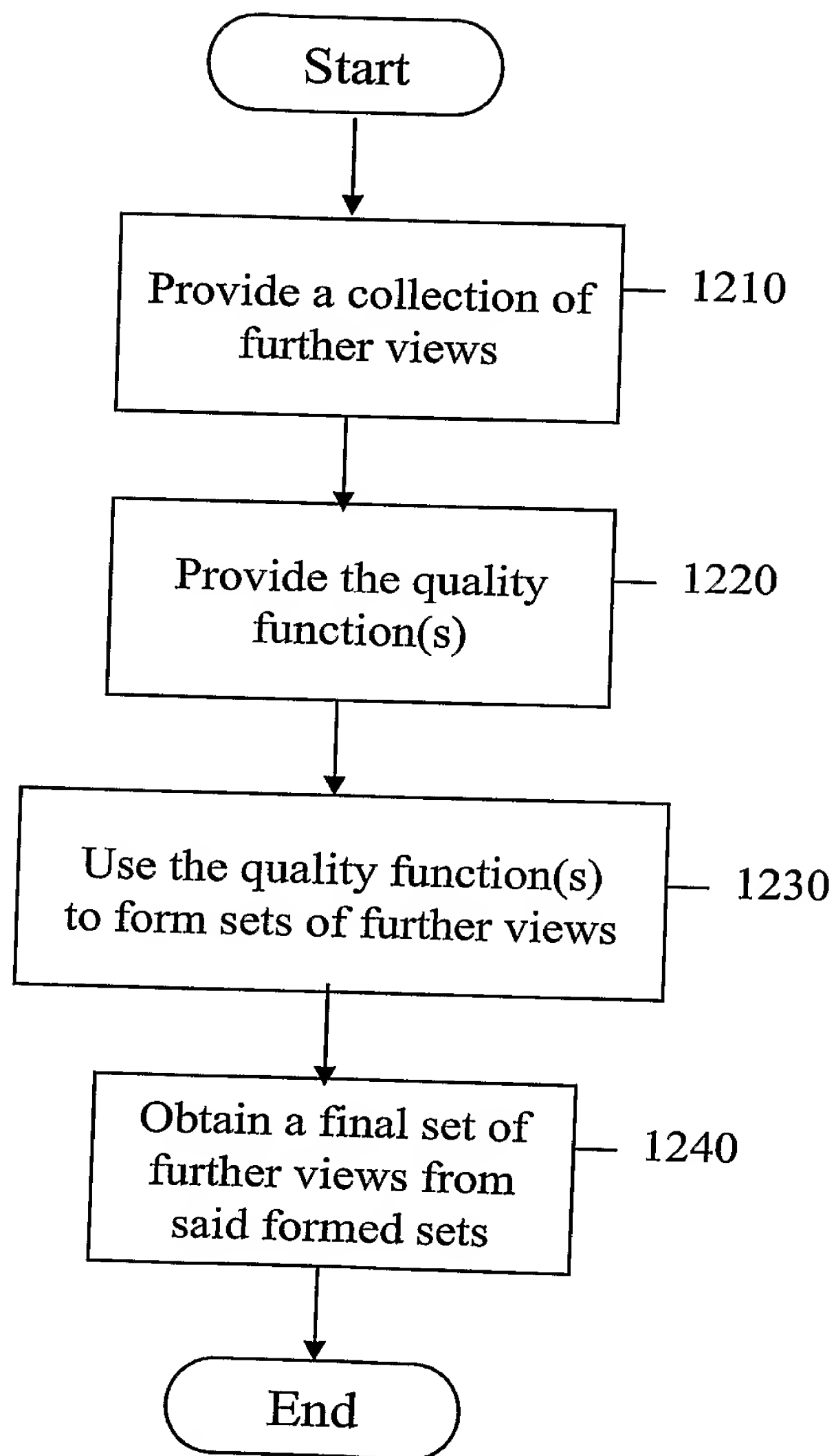
**Figure 86b**

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**Figure 87**

**Figure 88**

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**Figure 89**

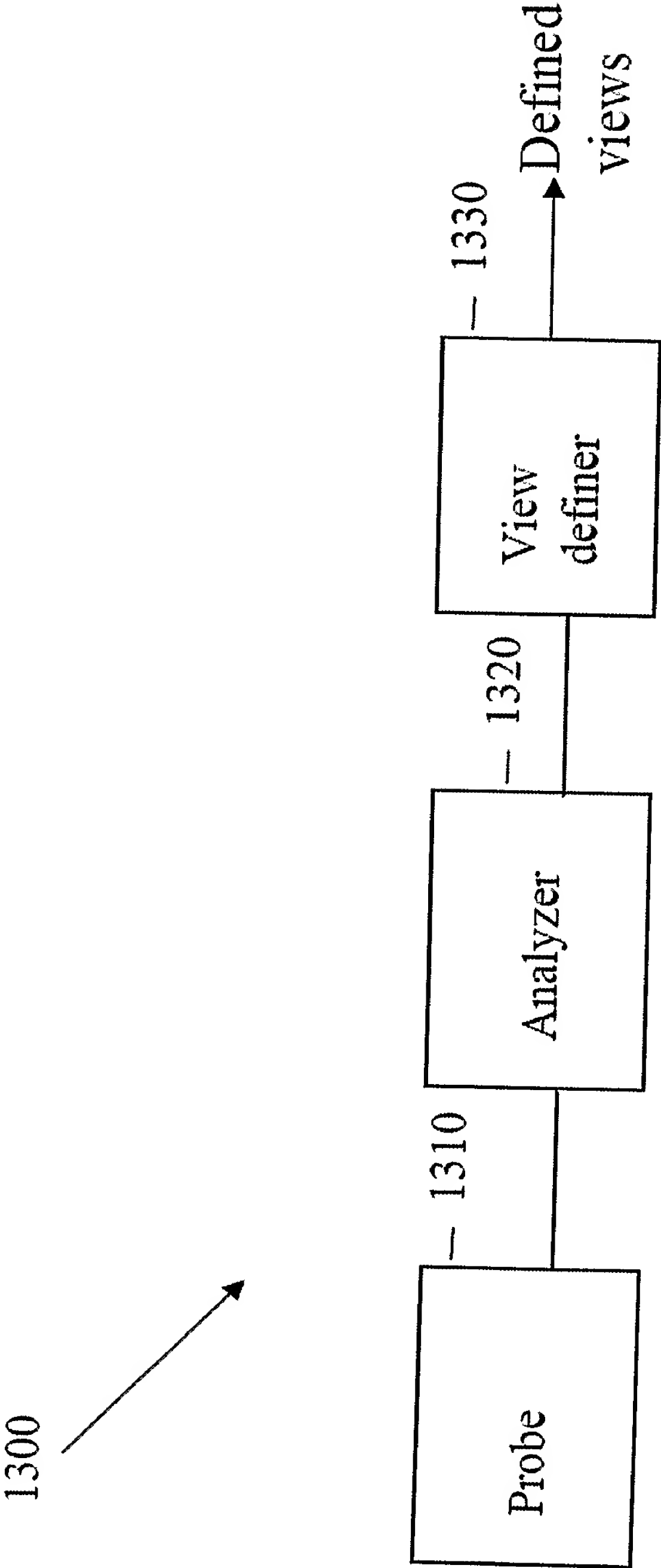
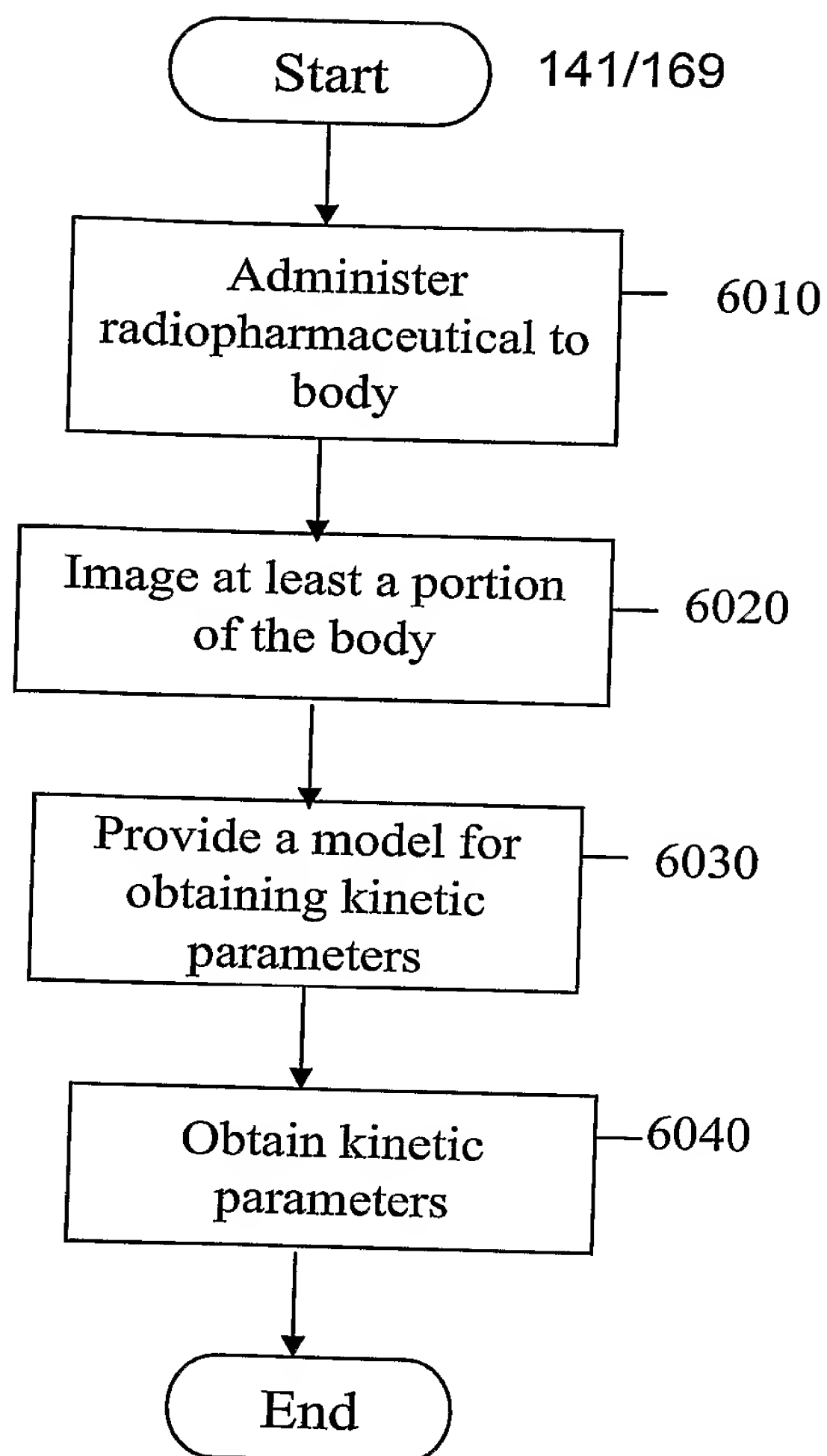


Fig. 90



**Figure 91**

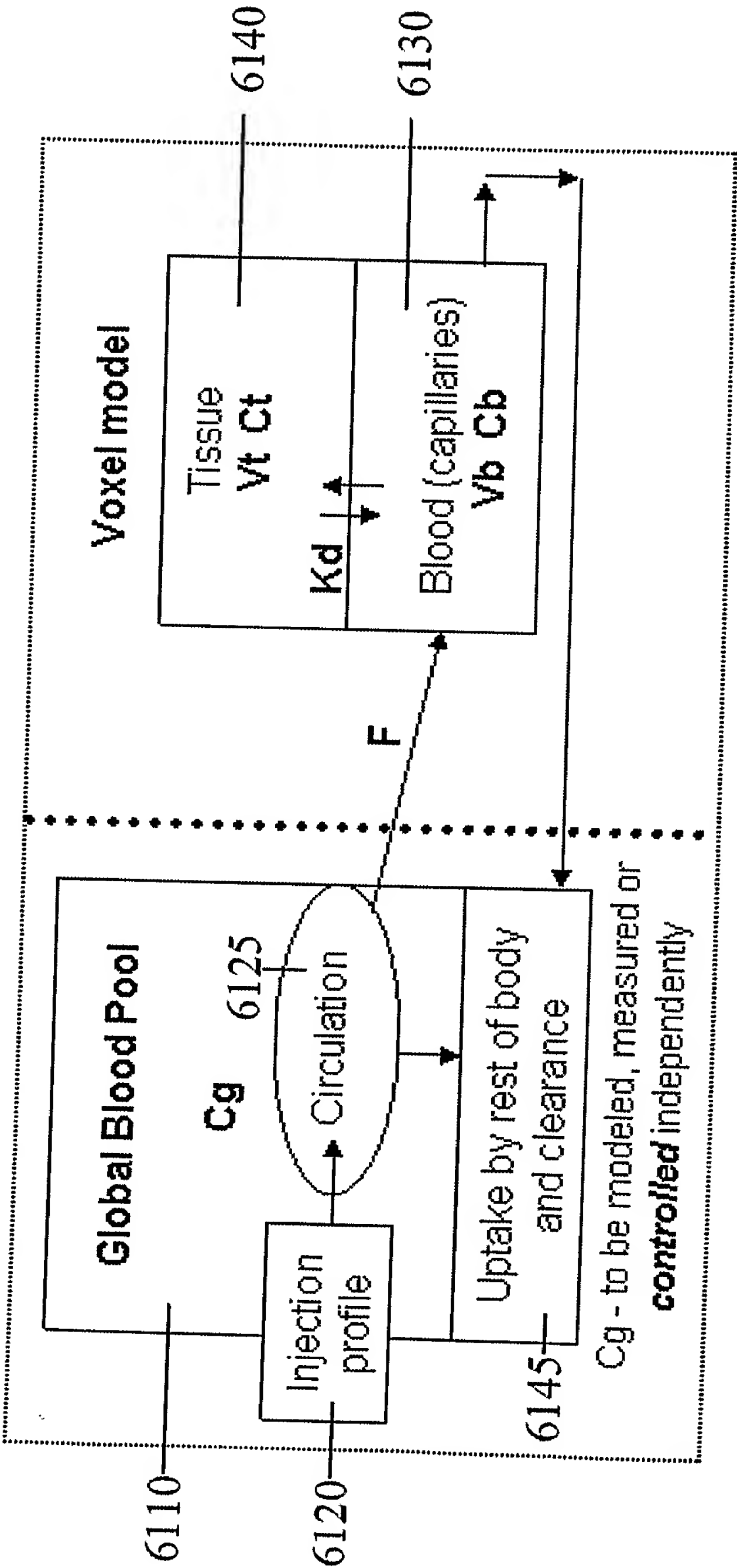


Fig. 92

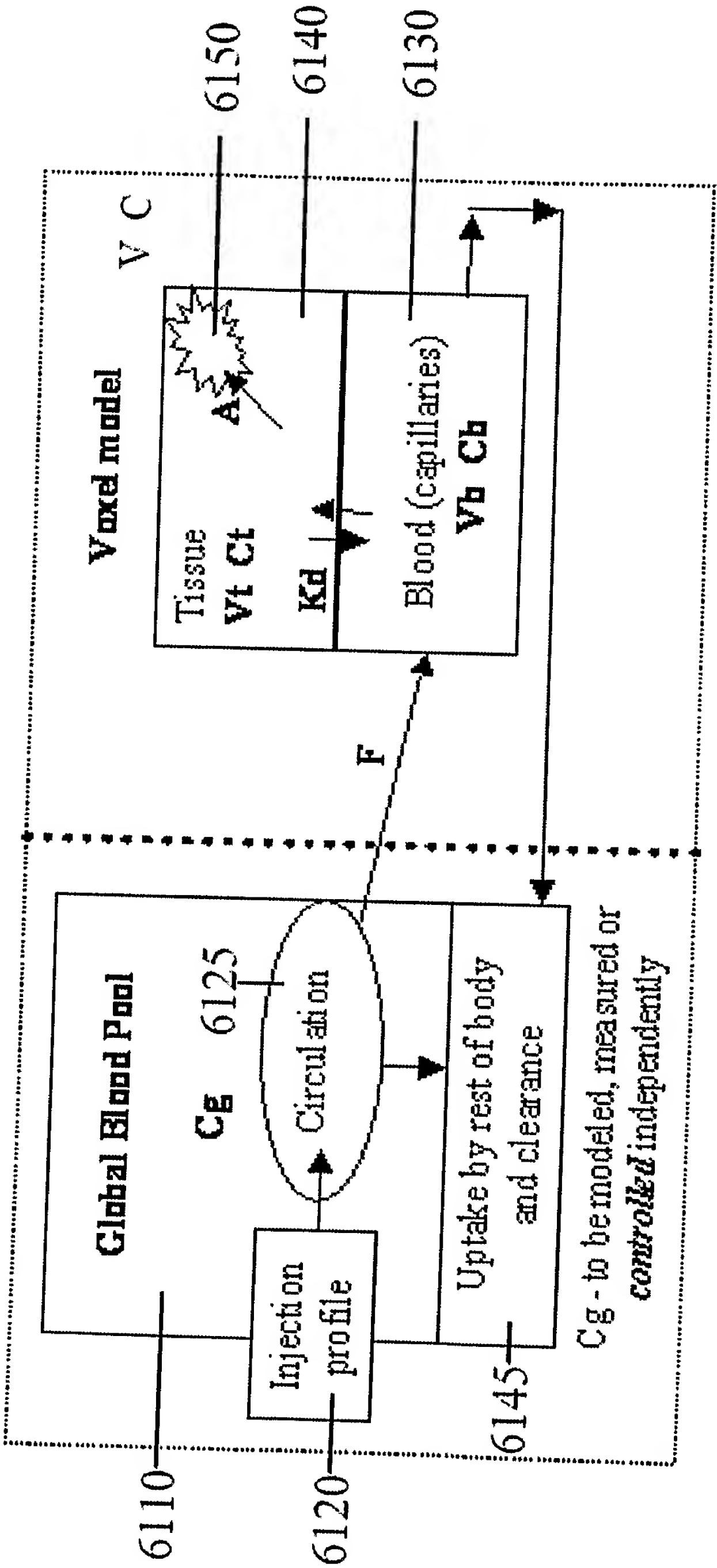


Fig. 93

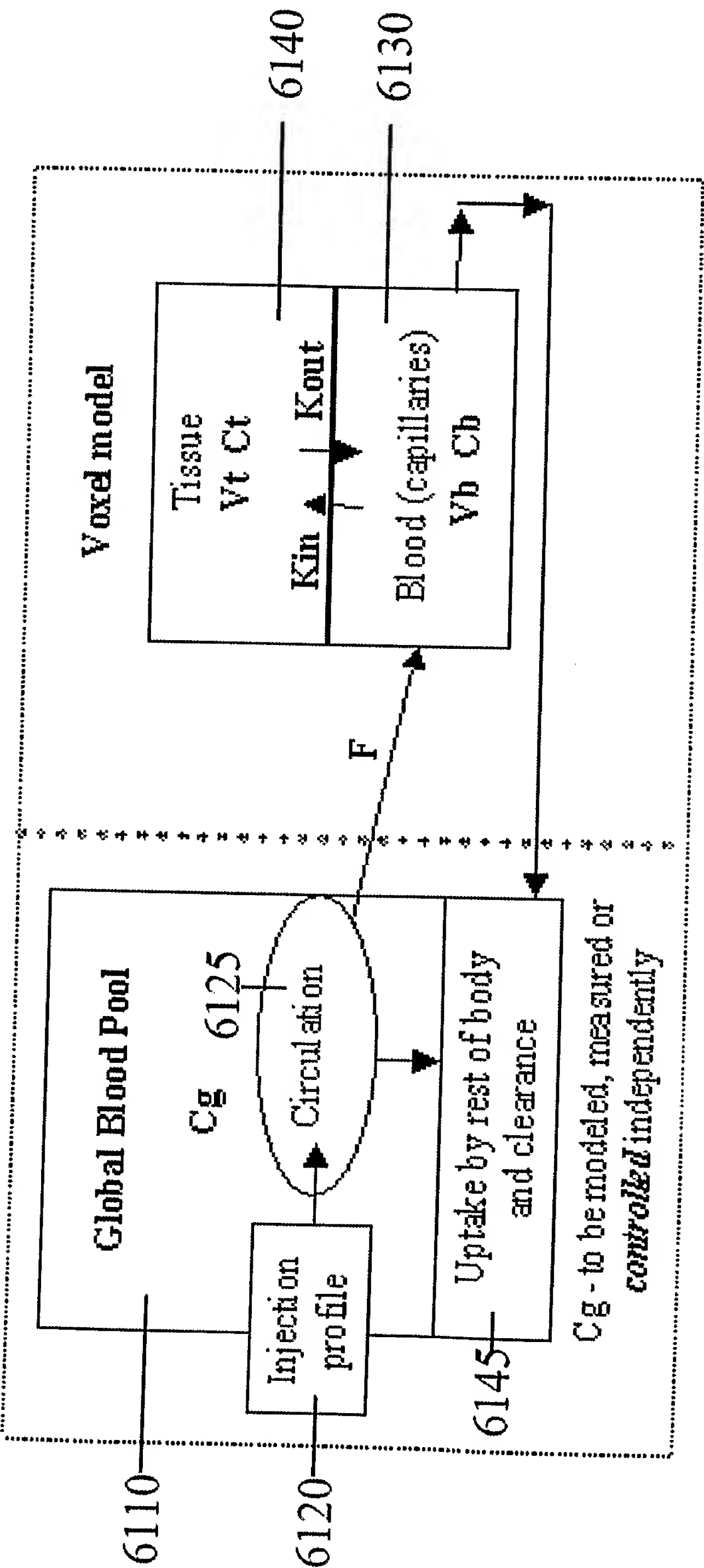
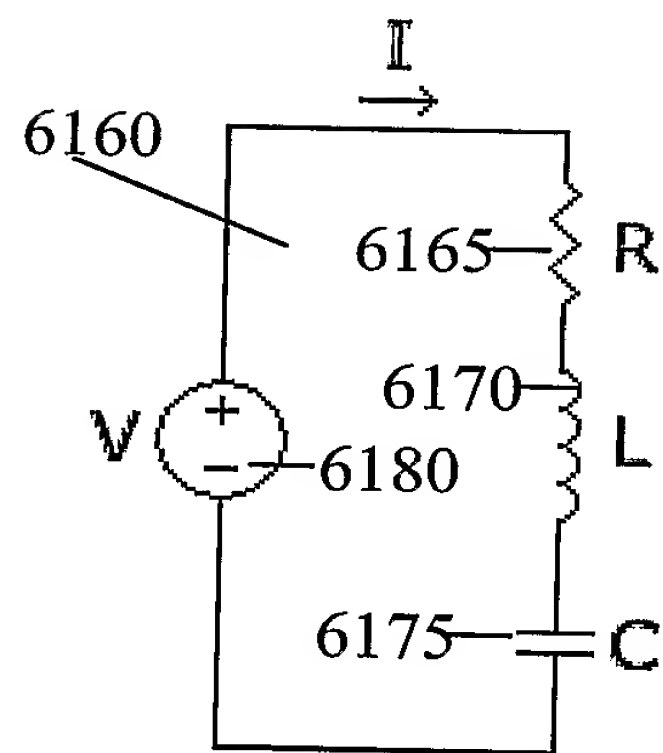
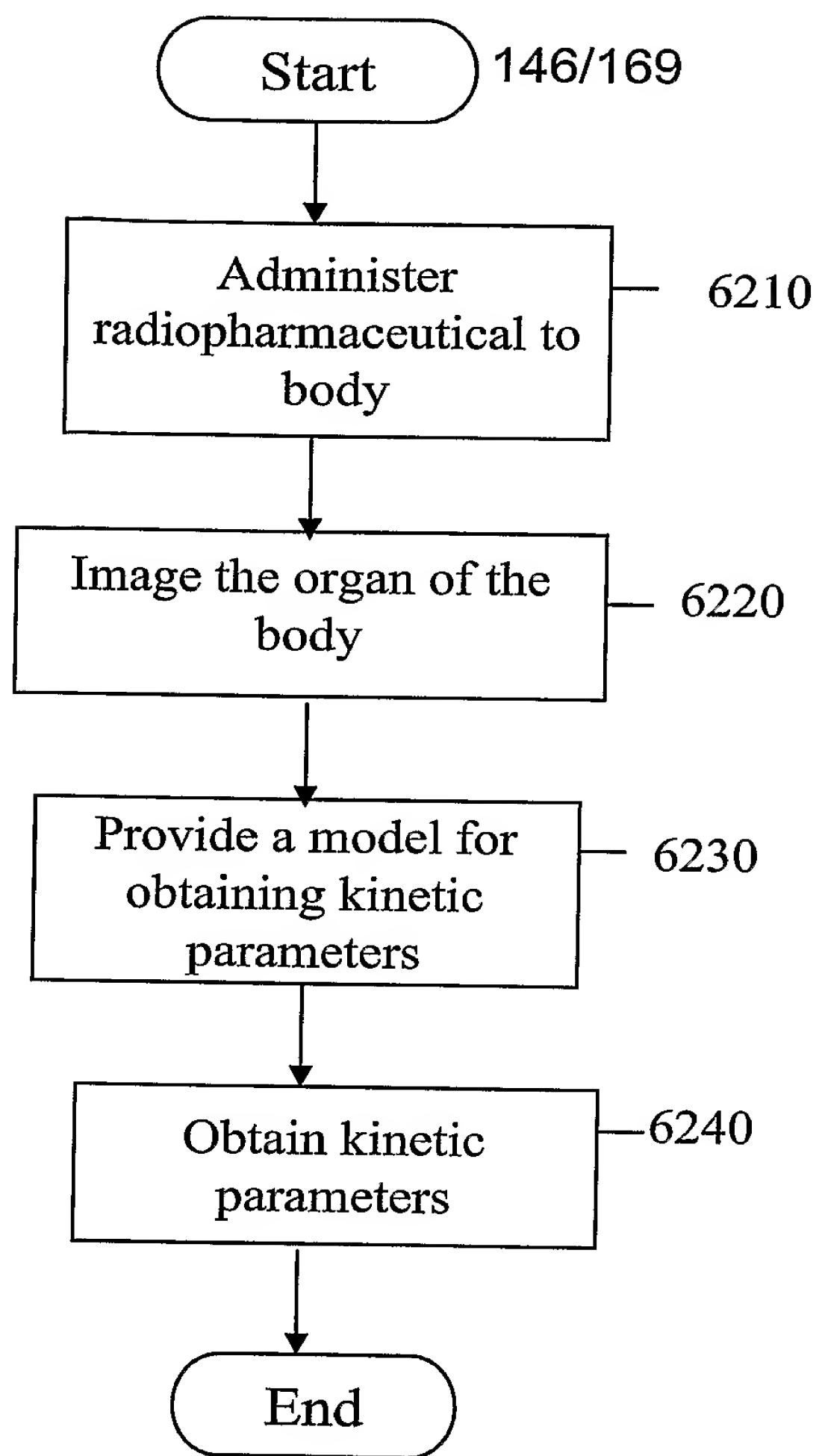


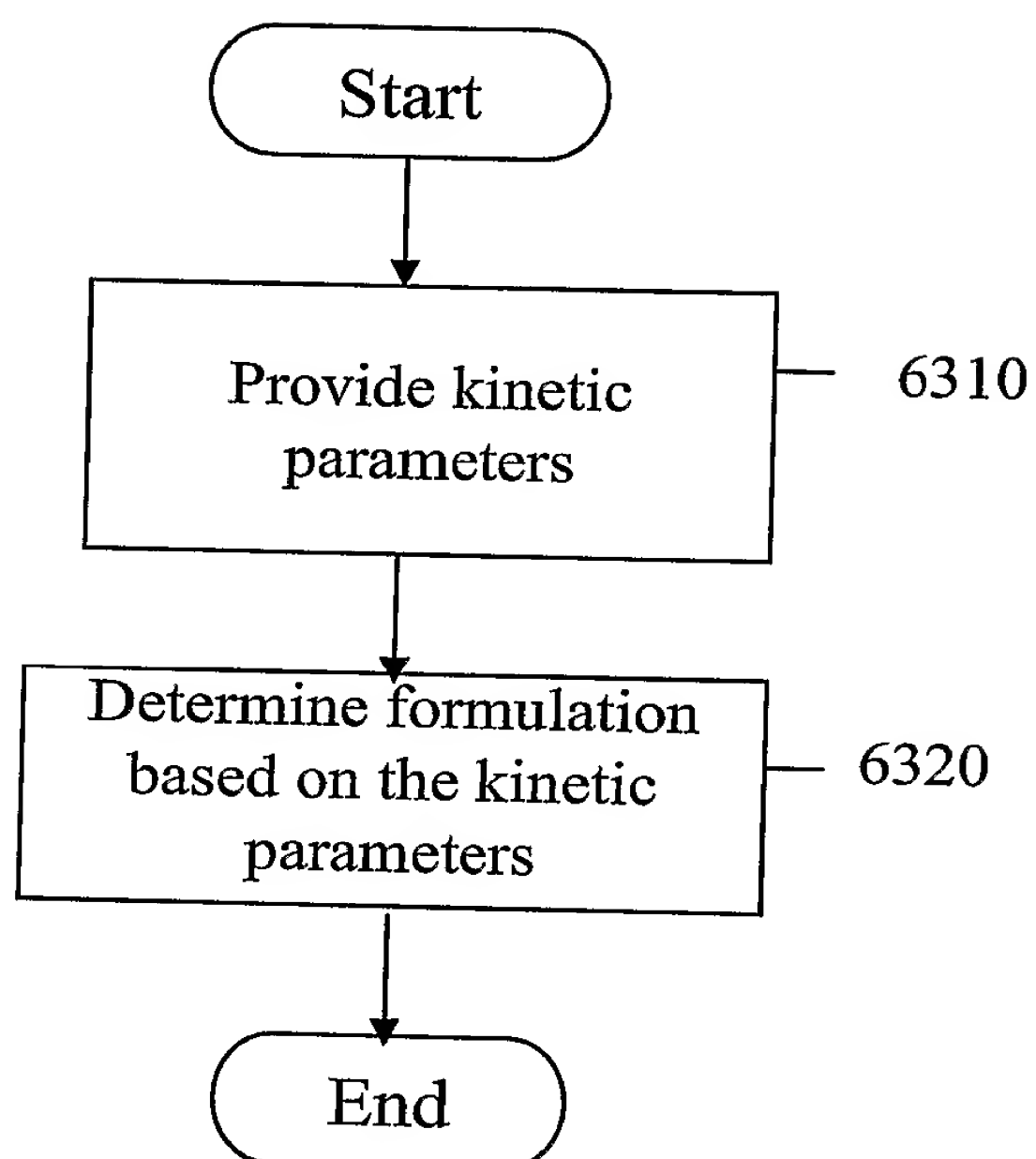
Fig. 94

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**Figure 95**

**Figure 96**

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**Figure 97**

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FIG. 98

Time (sec)	No. of events	Average rate (MHz)
0.001	56	0.056
0.002	369	0.369
0.003	379	0.379
0.004	378	0.378
0.005	382	0.382
0.006	376	0.376
0.007	366	0.366
0.008	372	0.372
0.009	374	0.374
0.010	372	0.372
0.011	370	0.370
0.012	371	0.371
0.013	364	0.364
0.014	372	0.372
0.015	374	0.374
0.016	372	0.372
0.017	364	0.364
0.018	368	0.368
0.019	364	0.364
0.020	373	0.373
0.021	362	0.362
0.022	374	0.374
0.023	372	0.372
0.024	377	0.377
0.025	367	0.367
0.026	377	0.377
0.027	373	0.373
0.028	363	0.363
0.029	373	0.373
0.030	370	0.370
0.031	370	0.370
0.032	370	0.370
0.033	378	0.378
0.034	372	0.372
0.035	380	0.380
0.036	372	0.372
0.037	373	0.373
0.038	373	0.373
0.039	375	0.375
0.040	372	0.372
0.041	379	0.379
0.042	373	0.373
0.043	374	0.374
0.044	368	0.368
0.045	370	0.370
0.046	373	0.373
0.047	369	0.369
0.048	372	0.372
0.049	372	0.372



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0.050	372	0.372
0.051	365	0.365
0.052	370	0.370
0.053	364	0.364
0.054	377	0.377
0.055	372	0.372
0.056	374	0.374
0.057	371	0.371
0.058	368	0.368
0.059	373	0.373
0.060	370	0.370
0.061	375	0.375
0.062	368	0.368
0.063	370	0.370
0.064	372	0.372
0.065	372	0.372
0.066	370	0.370
0.067	370	0.370
0.068	365	0.365
0.069	367	0.367
0.070	376	0.376

Fig. 98 Cont.

	REST PHASE				STRESS PHASE				
	INJECTION		WAITING TIME [MIN]	ACQUISITION DURATION [MIN]	STRESS	INJECTION		WAITING TIME [MIN]	GATED ACQUISITION DURATION [MIN]
	RP	DOSE [mCi]				RP	DOSE [mCi]		
SINGLE ISOTOPE/ LOW DOSE/FAST IMAGING	TL	<0.3	2	15	EXERCISE	TL	<3	10-15	1.5
DUAL ISOTOPE/ LOW DOSE/FAST IMAGING	TL	<0.3	2	15	EXERCISE	Tc- MIBI	30	30-60	1.5
GATED REST THALLIUM (STUNNING)	TL	1.5	2	5 (GATED)	EXERCISE	Tc- MIBI	30	30-60	1.5
THALLIUM STRESS PERFUSION	Tc- MIBI	3	30	1.5	PHARMA	TL	3	0	10 (DYNAMIC)
SIMULTANEOUS DUAL ISOTOPE STRESS PERFUSION	Tc- MIBI	3	20		EXERCISE/PHARMA	TL	3		10 (DYNAMIC)
DYNAMIC IMAGING	TL	0.3			PHARMA (ADENOSINE)	TL	3		10 (DYNAMIC)

Fig. 99A

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NO. PROTOCOL NAME	KEY FEATURES AND PROPERTIES	ADMINISTRATION PARAMETERS			DETECTOR PARAMETERS
		DOSE (mCi)	INJECTION PROFILE	INJECT TO ACQUISITION TIME	
A CARDIAC MAPPING	MIBI-TC, FAST, BEFORE LIVER UPTAKE	20-40	BOLUS	2 MIN, OR ADMIN UNDER THE CAMERA	140 KeV / 15%
B CARDIAC MAPPING	MIBI-TC AFTER LIVER UPTAKE	20-40	BOLUS	30+ MIN	140 KeV / 15%
C CARDIAC MAPPING	SIMULTANEOUS FAST DUAL-ISOTOPE TL-201+ LOW DOSE MIBI-TC	TL-201: 3.5-5; MIBI-Tc-99m: 4-8	2 BOLUS (BEFORE AND AT PEAK STRESS)	TL INJECTED PREVIOUSLY AT REST, TC UNDER CAMERA OR 2 MIN	Tc-140 KeV, Tl-72 KeV / 15%
D CARDIAC MAPPING	SIMULTANEOUS DUAL-ISOTOPE TL-201+ LOW DOSE MIBI-TC	TL-201: 3.5-5; MIBI-Tc-99m: 4-8	2 BOLUS (BEFORE AND AT PEAK STRESS)	SAME AS ONE OF FIRST 2 CARDIAC MAPPING PROTOCOLS	Tc-140 KeV, Tl-72 KeV / 15%
E CARDIAC MAPPING	SIMULTANEOUS DUAL-ISOTOPE FULL TL-201+ FULL DOSE MIBI-TC	TL-201: 3.5-5; MIBI-Tc-99m: 20-40	2 BOLUS (BEFORE AND AT PEAK STRESS)	SAME AS ONE OF PROTOCOLS A OR B	Tc-140 KeV, Tl-167 KeV / 10%
F CARDIAC MAPPING - UNDERWEIGHT (BMI<18.5)	MIBI-TC-99M AFTER LIVER UPTAKE	15-20	BOLUS	30+ MIN	140 KeV / 15%
G1 CARDIAC MAPPING - NORMAL (18.6<BMI<24.9)	MIBI-TC-99M AFTER LIVER UPTAKE	20-30	BOLUS	30+ MIN	140 KeV / 10%
G2 CARDIAC MAPPING - OVERWEIGHT (25<BMI<29.9)	MIBI-TC-99M AFTER LIVER UPTAKE	30-35	BOLUS	30+ MIN	140 KeV / 10%

Fig. 99B

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SCANNING PARAMETERS										ANALYSIS PARAMETERS		
NO.	TOTAL SCAN TIME	COLUMNS DIFFERENCES / UNIFORM SCAN	ANGULAR RANGE	TOTAL # ANGULAR ORIENTATIONS	ANGULAR STEP / INTERLACE	DWELL TIME	GATED ANALYSIS OF VOLUMES	ANALYSIS ALGORITHM / PARAMETERS				
A	120 SEC	a) 4 X OUTER b) 6 X INNER	a) 40-60 DEG b) 90-120 DEG	120X10	a) 0.3-0.5 DEG b) 0.75-1 DEG	1 SEC	YES, 16-32 FRAMES	INTENSITY IMAGE, EJECTION FRACTION				
B	120 SEC	a) 4 X OUTER b) 6 X INNER	a) 40-60 DEG b) 90-120 DEG	120X10	a) 0.3-0.5 DEG b) 0.75-1 DEG	1 SEC	YES, 16-32 FRAMES	INTENSITY IMAGE, EJECTION FRACTION				
C	120 SEC	a) 4 X OUTER b) 6 X INNER	a) 40-60 DEG b) 90-120 DEG	120X10	a) 0.3-0.5 DEG b) 0.75-1 DEG	1 SEC	YES, 16-32 FRAMES	INTENSITY IMAGE, EJECTION FRACTION				
D	120 SEC	a) 4 X OUTER b) 6 X INNER	a) 40-60 DEG b) 90-120 DEG	120X10	a) 0.3-0.5 DEG b) 0.75-1 DEG	1 SEC	YES, 16-32 FRAMES	INTENSITY IMAGE, EJECTION FRACTION				
E	UP TO 1200 SEC	a) 4 X OUTER b) 6 X INNER	a) 40-60 DEG b) 90-120 DEG	240X10	a) 0.15-0.25 DEG b) 0.375-0.5 DEG	5 SEC	YES, 16-32 FRAMES	INTENSITY IMAGE, EJECTION FRACTION				
F	90 SEC	a) 4 X OUTER b) 6 X INNER	a) 20-35 DEG b) 45-60 DEG	60X10	a) .3-.75 DEG b) 0.75-1 DEG	1 SEC	YES, 16-32 FRAMES	INTENSITY IMAGE, EJECTION FRACTION				
G1	120 SEC	a) 4 X OUTER b) 6 X INNER	a) 30-45 DEG b) 75-90 DEG	120X10	a) 0.5-0.75 DEG b) 0.625-1 DEG	1.5 SEC	YES, 16-32 FRAMES	INTENSITY IMAGE, EJECTION FRACTION				
G2	120 SEC	a) 4 X OUTER b) 6 X INNER	a) 40-60 DEG b) 90-120 DEG	120X10	a) 0.3-0.5 DEG b) 0.75-1 DEG	2 SEC	YES, 16-32 FRAMES	INTENSITY IMAGE, EJECTION FRACTION				

Fig. 99C

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NO.	PROTOCOL NAME	KEY FEATURES AND PROPERTIES	ADMINISTRATION PARAMETERS			DETECTOR PARAMETERS
			DOSE (mCi)	INJECTION PROFILE	INJECT TO ACQUISITION TIME	
H	CARDIAC MAPPING - OBESE (BMI>30)	MIBI-TC AFTER LIVER UPTAKE	35-40	BOLUS	30+ MIN	140 KeV / 6%
I	CARDIAC DYNAMIC MAPPING	TEBOROXIME-TC	20-40	BOLUS	-1 MIN (IMAGE BEFORE INJECT), OR SIMULTANEOUSLY WITH INJECT	140 KeV / 15%
J	CARDIAC DYNAMIC MAPPING (2-STEP)	TEBOROXIME-TC	20-40	(i) INITIAL SMALL BOLUS FOR IDENTIFYING ROI, (ii) FULL BOLUS FOR DYNAMIC STUDY	(i) 5+ MIN (ii) -1 MIN (IMAGE BEFORE INJECT)	140 KeV / 15%
K	TUMOR SCAN (MULTIPLE BODY SEGMENTS - HEAD TO LEGS)	MDP-TC-99M AFTER LIVER UPTAKE	20-40	BOLUS	30+ MIN	140 KeV / 15%
L	TUMOR SCAN (MULTIPLE BODY SEGMENTS - HEAD TO LEGS), FOCUSED SCAN	MDP-TC-99M AFTER LIVER UPTAKE	20-40	BOLUS	30+ MIN	140 KeV / 15%
M	TUMOR SCAN WITH COCKTAIL (MULTIPLE BODY SEGMENTS - HEAD TO LEGS), FOCUSED SCAN	FDG (METABOLISM), MIBI-TC-99M AND TL (PERFUSION)	TL-201: 3.5-5; MIBI-TC-99M: 20-40; 18-F FDG 10-30	BOLUS	30+ MIN	Tc-140 KeV, Tl-72 KeV, FDG 511 KeV / 10%

Fig. 99D

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NO.	SCANNING PARAMETERS						ANALYSIS PARAMETERS	
	TOTAL SCAN TIME	COLUMNS DIFFERENCES / UNIFORM SCAN	ANGULAR RANGE	TOTAL # ANGULAR ORIENTATIONS	ANGULAR STEP / INTERLACE	DWELL TIME	GATED ANALYSIS OF VOLUMES	ANALYSIS ALGORITHM / PARAMETERS
H	180 SEC	a) 4 X OUTER b) 6 X INNER	a) 40-60 DEG b) 90-120 DEG	160X10	a) 0.25-0.375 DEG b) 0.6-0.75 DEG	1.2 SEC	YES, 8-16 FRAMES	INTENSITY IMAGE, EJECTION FRACTION
I	<= 600 SEC	a) 2 X OUTER b) 8 X INNER	a) 40-60 DEG b) 90-120 DEG	600X10	a) continuous b) continuous INTERLACED SCAN	1 SEC	YES, 8 FRAMES	KINETIC PARAMETERS, PREDEFINED PATHOLOGICAL VALUES
J	(i) 60 SEC FOR IDENTIFYING ROI (ii) 600 SEC DYNAMIC STUDY	a) 2 X OUTER b) 8 X INNER	a) 40-60 DEG b) 90-120 DEG	(i) 60X10 (ii) 600X10	(i) a) 0.75-1 DEG b) 0.75-0.75-1 DEG (ii) a) continuous b) continuous INTERLACED SCAN	1 SEC	YES, 8 FRAMES	KINETIC PARAMETERS, PREDEFINED PATHOLOGICAL VALUES
K	240 SEC PER BODY SEGMENT	16	40-60 DEG	120X16	0.3-0.5 DEG	2 SEC	NO	INTENSITY IMAGE, PREDEFINED PATHOLOGICAL VALUES
L	(i) 120 SEC PER BODY SEGMENT (ii) 60 SEC PER ROI	16	(i) 45-60 DEG (ii) 15-20 DEG	(i) 120X16 (ii) 60x16	(i) 0.375-0.5 DEG (ii) 0.25-0.3	1 SEC	NO	INTENSITY IMAGE, PREDEFINED PATHOLOGICAL VALUES
M	(i) 120 SEC PER BODY SEGMENT (ii) 60 SEC PER ROI	16	(i) 45-60 DEG (ii) 15-20 DEG	(i) 120X16 (ii) 60x16	(i) 0.375-0.5 DEG (ii) 0.25-0.4	1 SEC	NO	INTENSITY IMAGE, PREDEFINED PATHOLOGICAL VALUES

Fig. 99E

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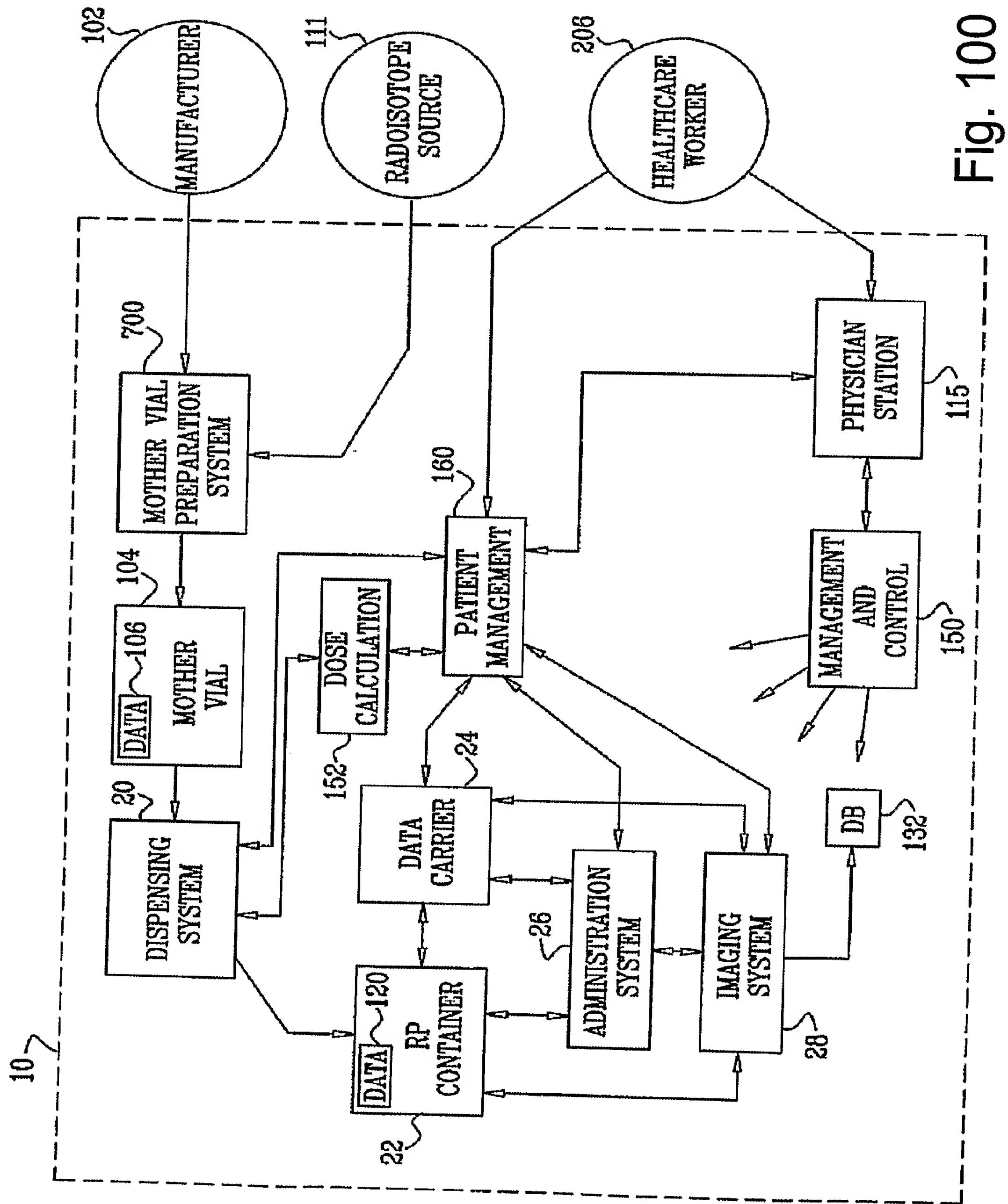


Fig. 100

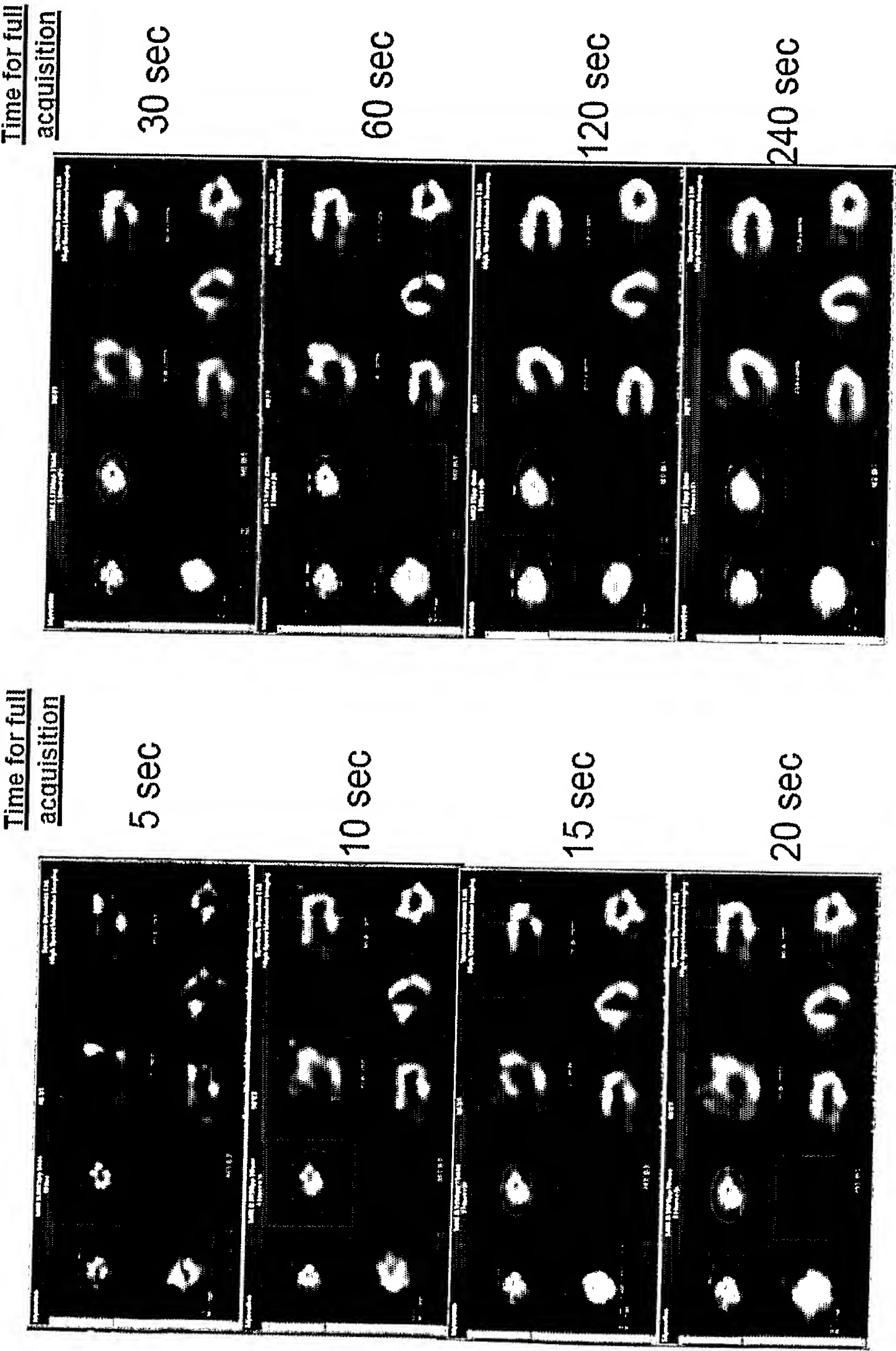
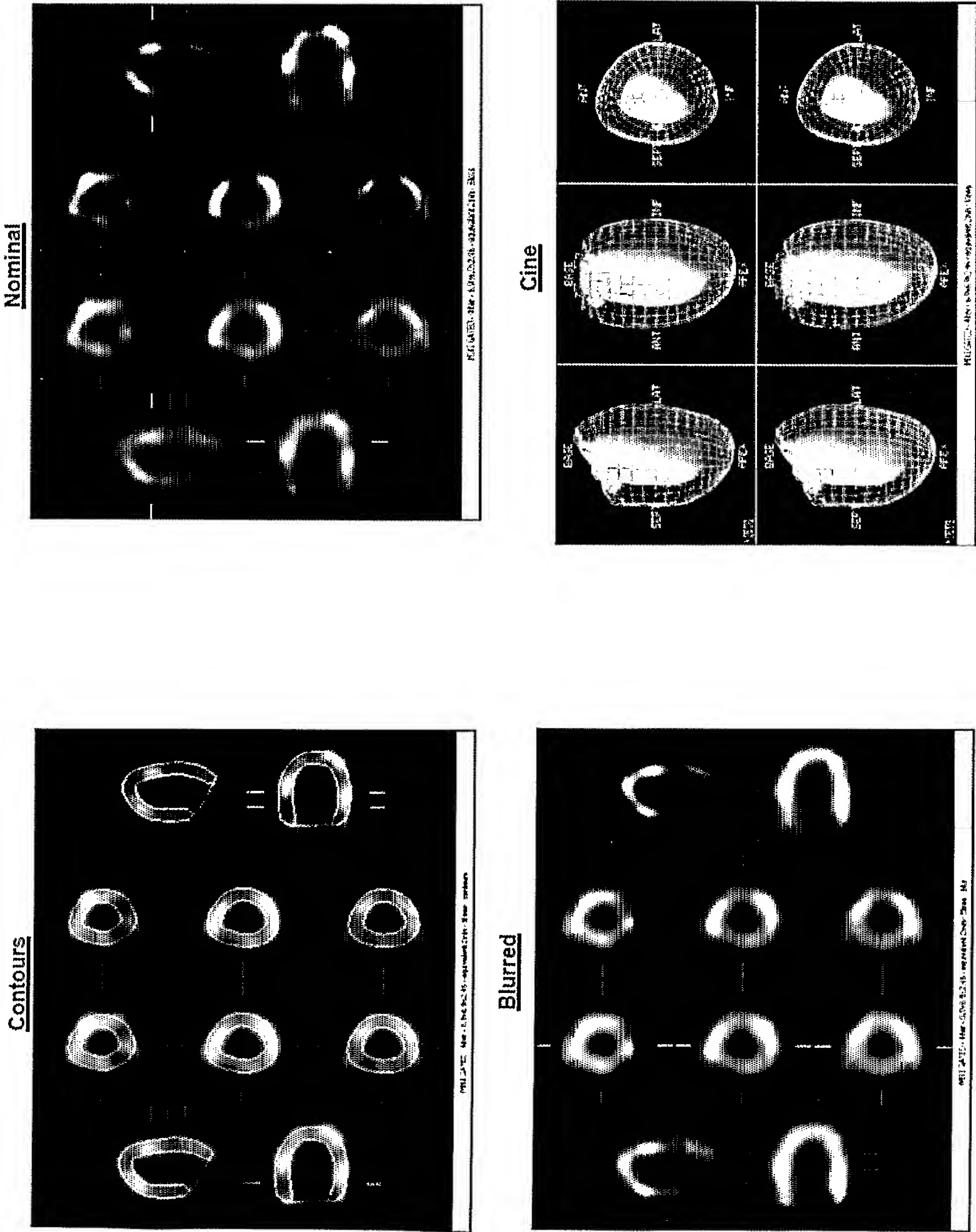


Fig. 101A

Real patient study-Time slices



Fig. 101B



Dual Isotope- no defect, TI window

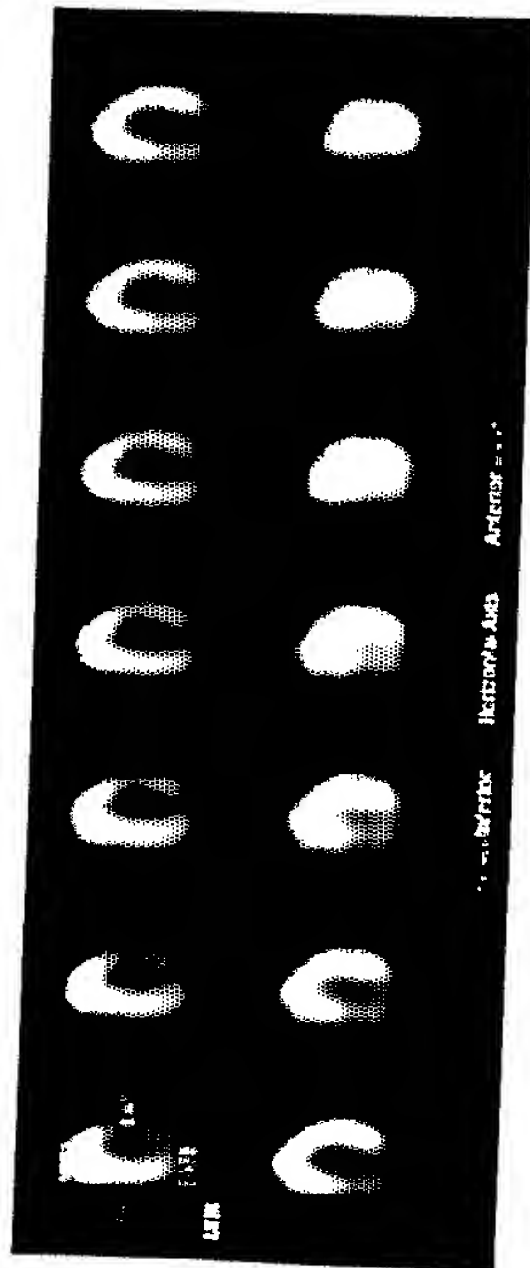


Fig. 101C

Dual Isotope- 2cm Tc99m-filled insert- Tc99m window

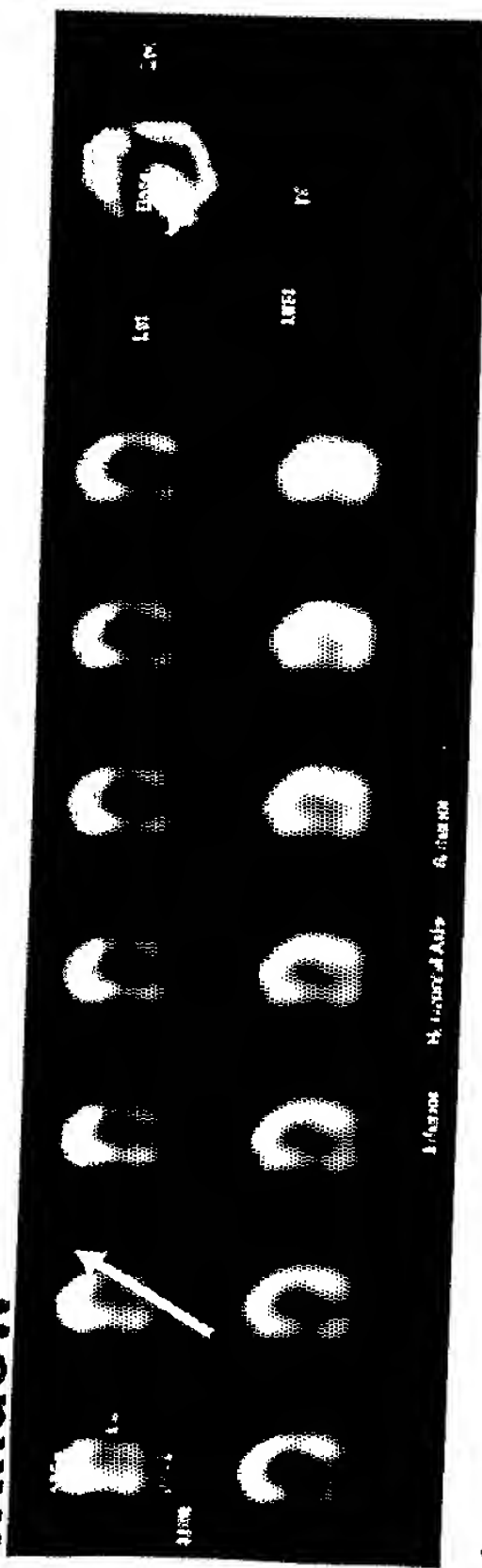


Fig. 101D

Apparent perfusion defect where insert is placed- the insert is filled with Tc99m, but the wall of the insert makes up for ~30% of its volume and therefore is not filled with Tc-99m- this theoretically simulates a ~30% "perfusion defect" ~30% "perfusion defect" cannot be resolved in conventional camera

Dual Isotope- 2cm Tc99m-filled insert- TI-201 window

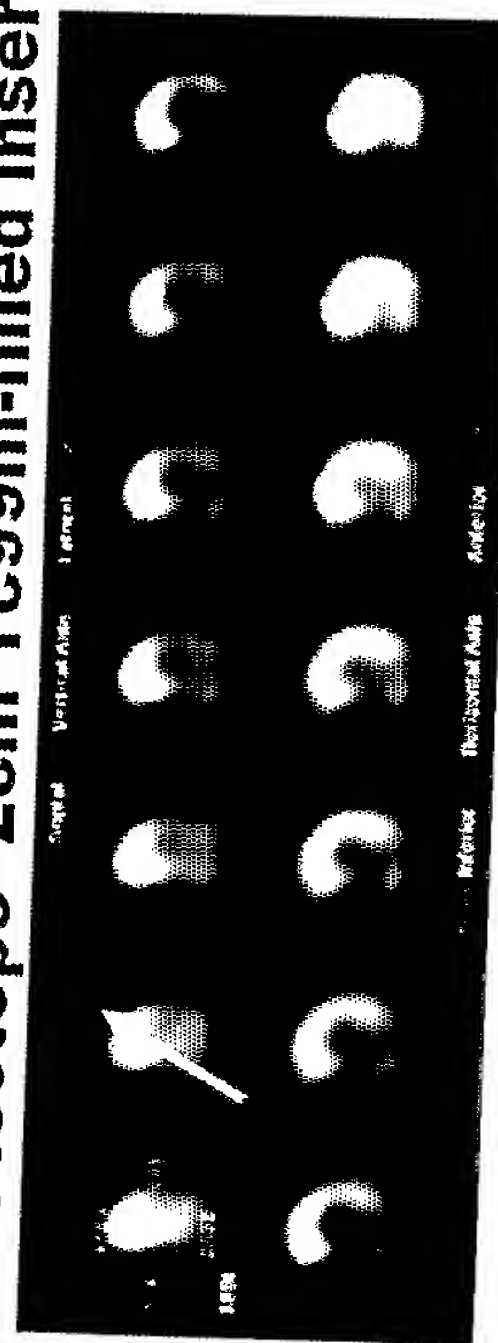


Fig. 101E

Dual Isotope- 2cm Tc99m-  
filled insert- Tl-201 window

D-SPECT Camera

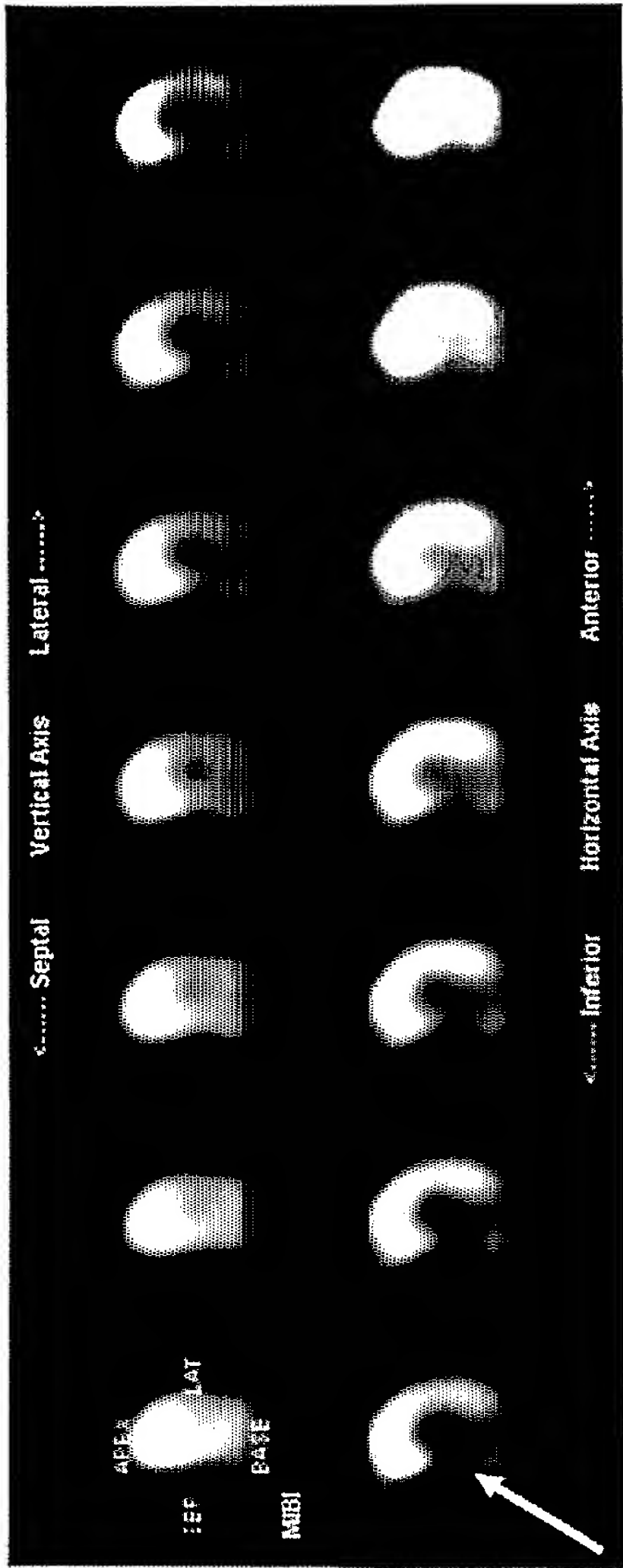


Fig. 101F

# Dual Isotope- Tl-201 window

D-SPECT - No insert

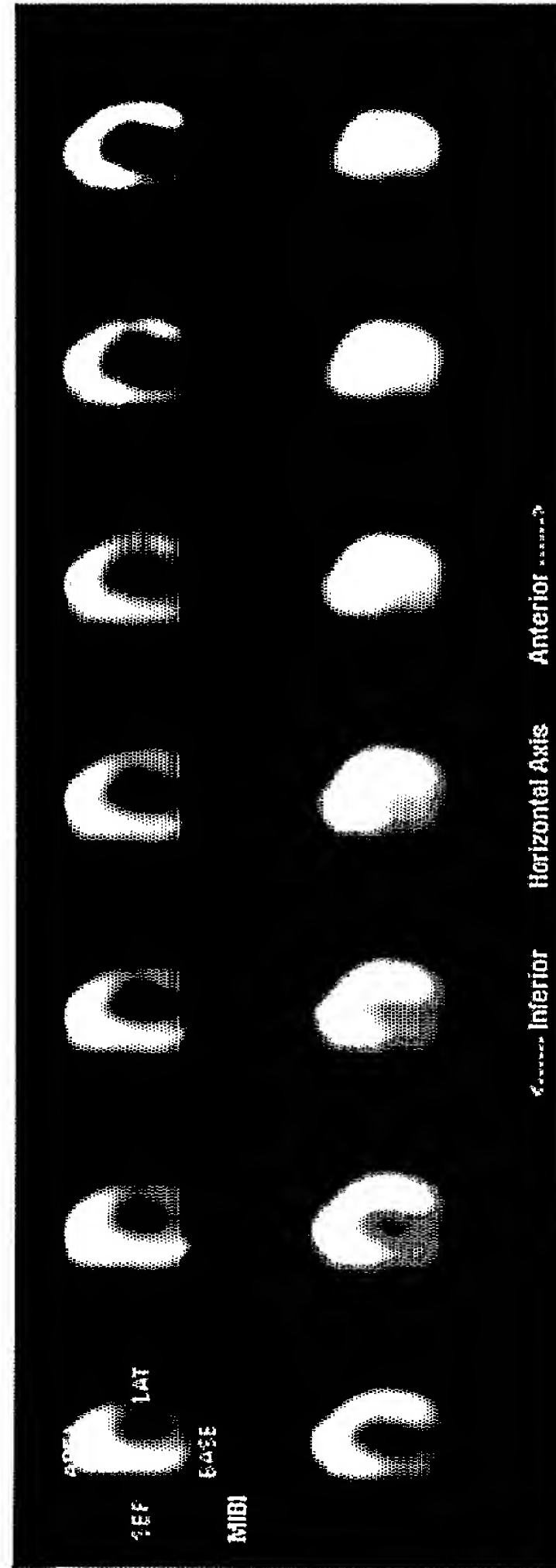


Fig. 101G



D-SPECT -2cm insert

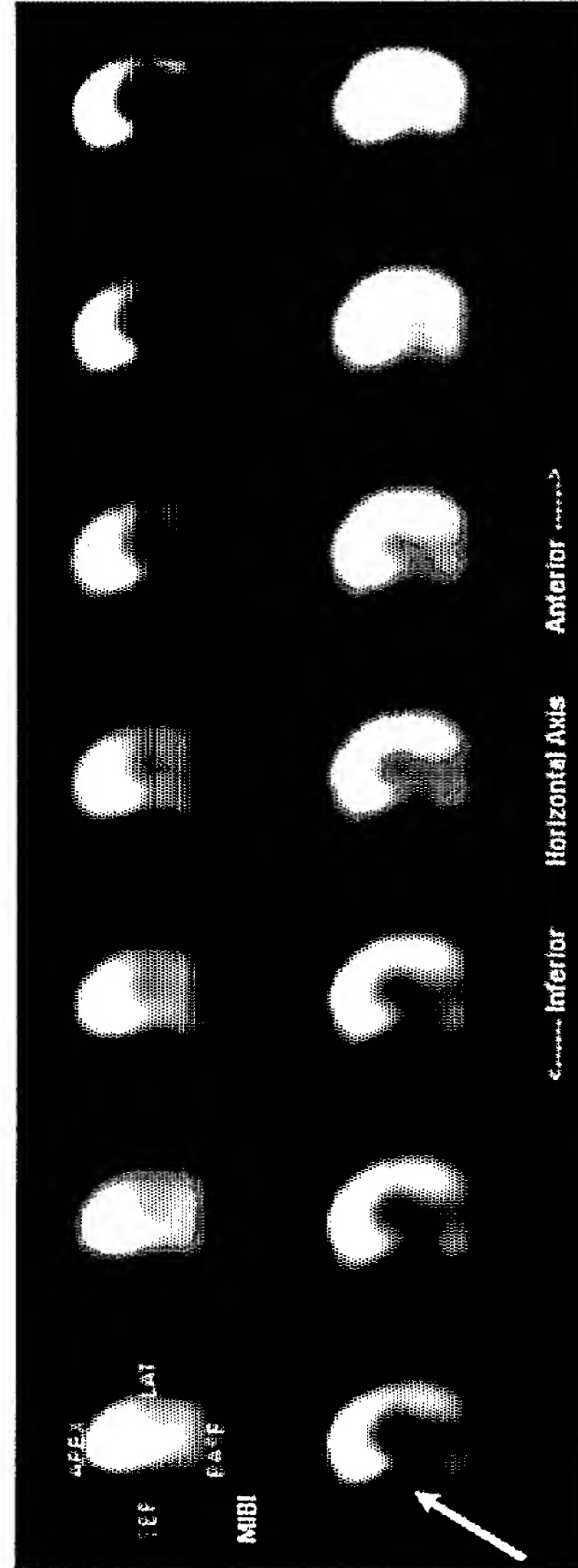
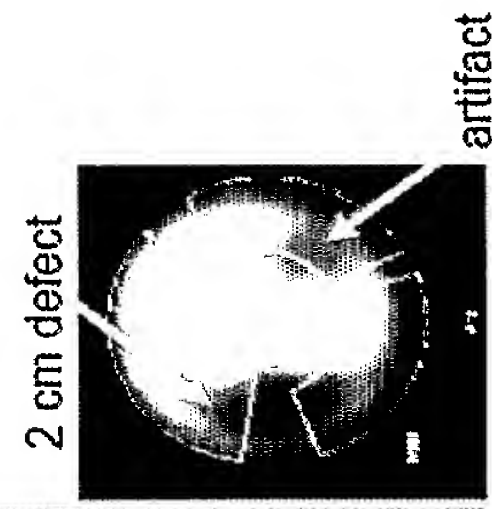


Fig. 101H



2 cm defect

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# FIGS. 102A-B

Conventional SPECT  
60 min post injection

A



D-SPECT

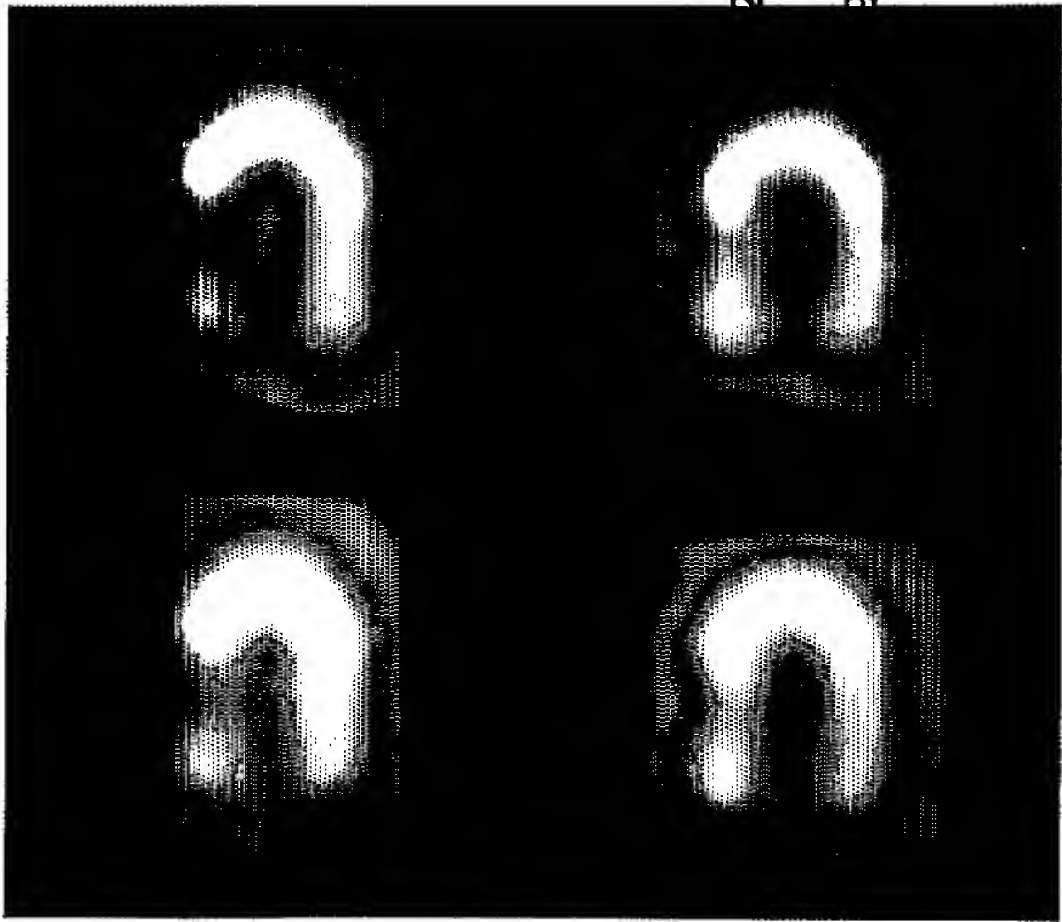
Immediate post injection

B



FIGs. 103A-B

A

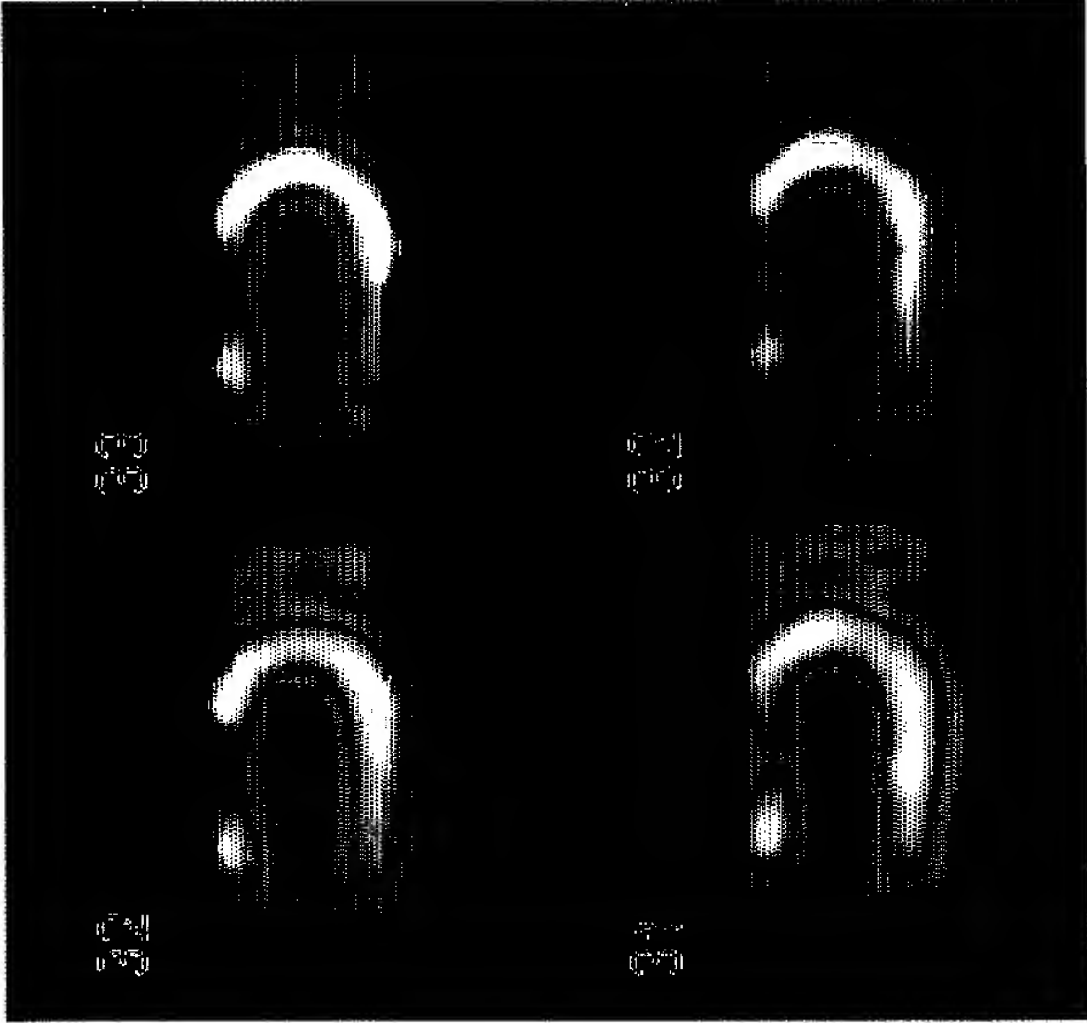


$^{201}\text{Tl}$   
alone

$^{201}\text{Tl}$  with  
 $^{99\text{m}}\text{Tc}$  crosstalk

Conventional Spect

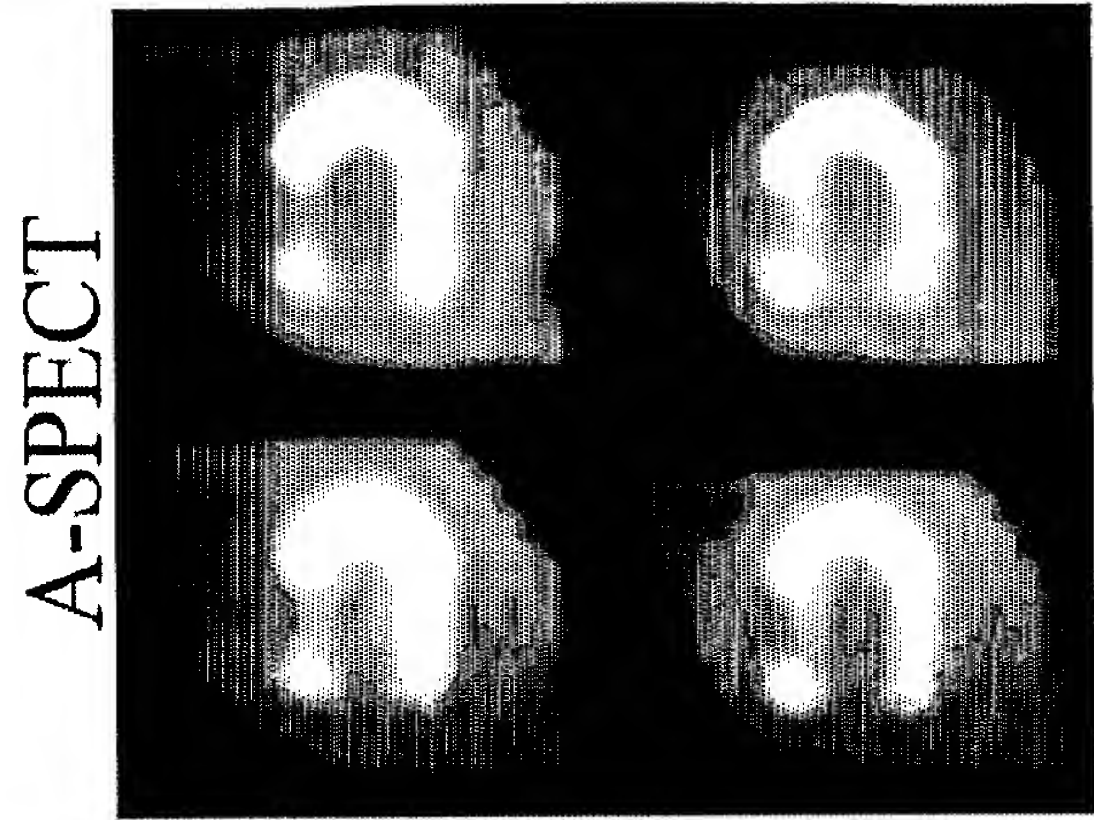
B



Spect according to the  
present invention

Fig. 104B

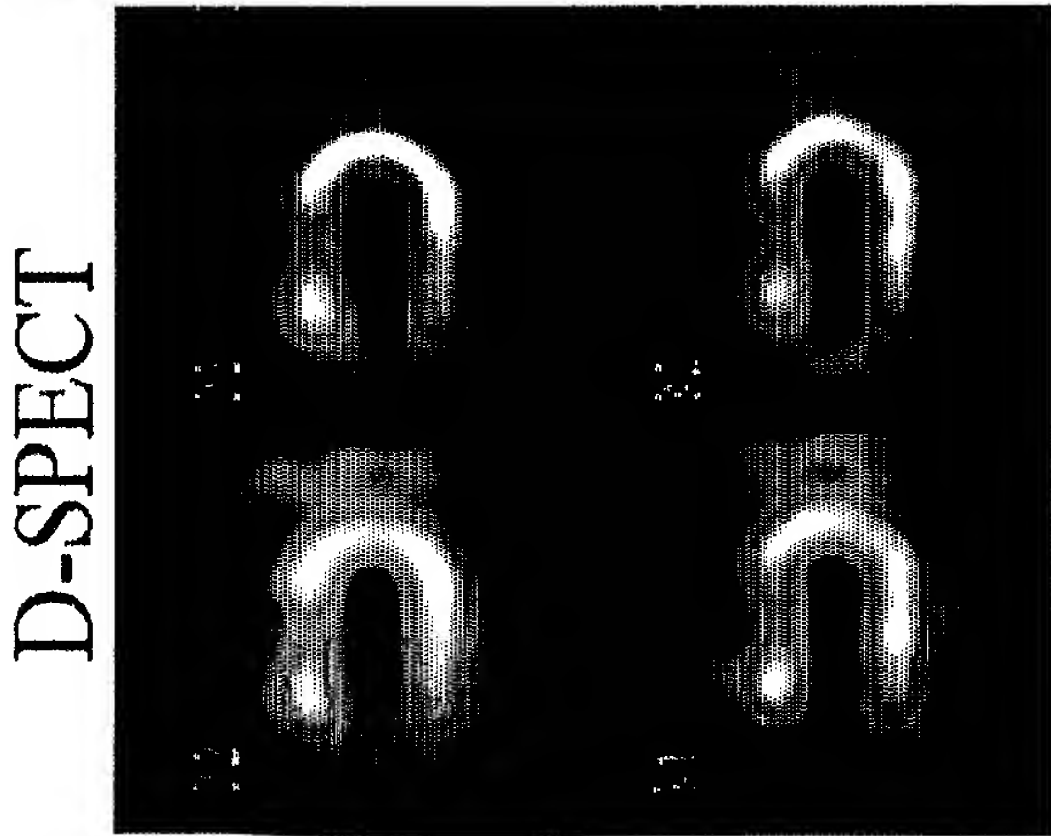
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Virgin Thallium

Simultaneous  
Dual Thallium

Fig. 104A



## FIG. 105

### PHANTOM SET-UP:

- Anthropomorphic torso phantom + 2cm defect filled with water
- “Virgin” Tl protocol :  
 LV = 0.15mCi Tl at 10:24  
 Liver = 0.51mCi Tl at 10:28  
 Background = 1.00mCi Tl at 10:33
- Simultaneous dual protocol (Tc added to Tl) :  
 LV = 0.16mCi Tc at 12:41  
 Liver = 1.00mCi Tc at 12:39  
 Background = 0.64mCi Tc at 12:37

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### D-SPECT SCAN PROTOCOL:

- 120positions – 1spp – 2min scan
- 120positions – 2spp – 4min scan
- 120positions – 3spp – 6min scan



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MACHINE:

- GE Millennium VG (Tl → -15%;+15% on 72keV + -10%;+10% on 167keV  
Tc → -10%;+10% on 140keV)

PHANTOM SET-UP:

- Anthropomorphic phantom + 2cm anterior defect filled with water
- “Virgin” Tl protocol :      LV = 0.15mCi Tl  
                                    Liver = 0.5mCi Tl  
                                    Background = 1.00mCi Tl
- Simultaneous dual protocol (Tc added to Tl) :      LV = 0.15mCi Tc  
  Liver = 1.00mCi Tc  
  Background = 0.65mCi Tc

ACQUISITION PROTOCOL:

- 30positions per head – 30spp – 15min scan – 8.9MC
- 30positions per head – 60spp – 30min scan – 4.7MC

RECONSTRUCTION:

Standard cardiac reconstruction protocol : 2 iterations - 10 subsets –  
butterworth(0.4;10)

Fig. 106

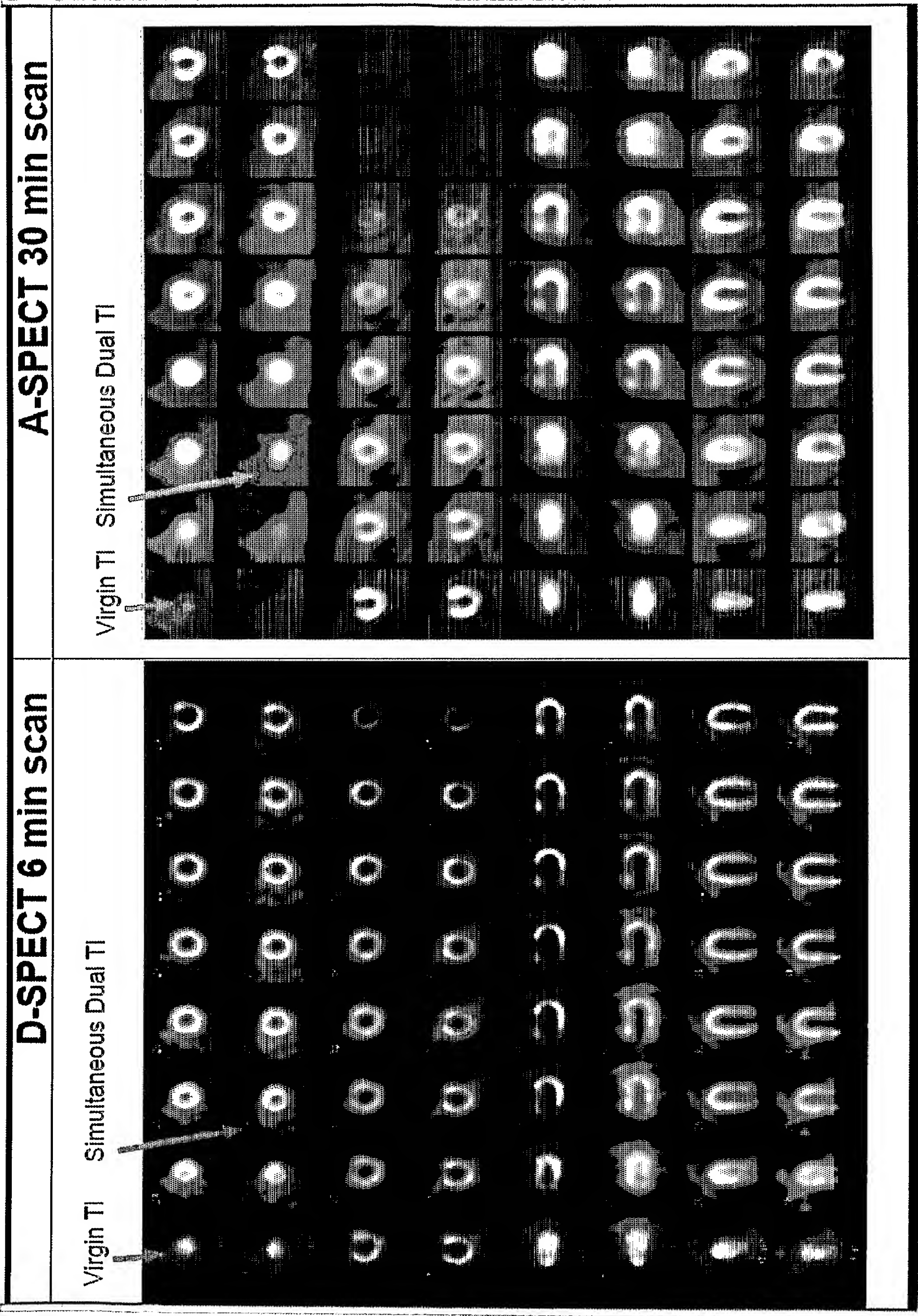


Fig. 107A

Fig. 107B

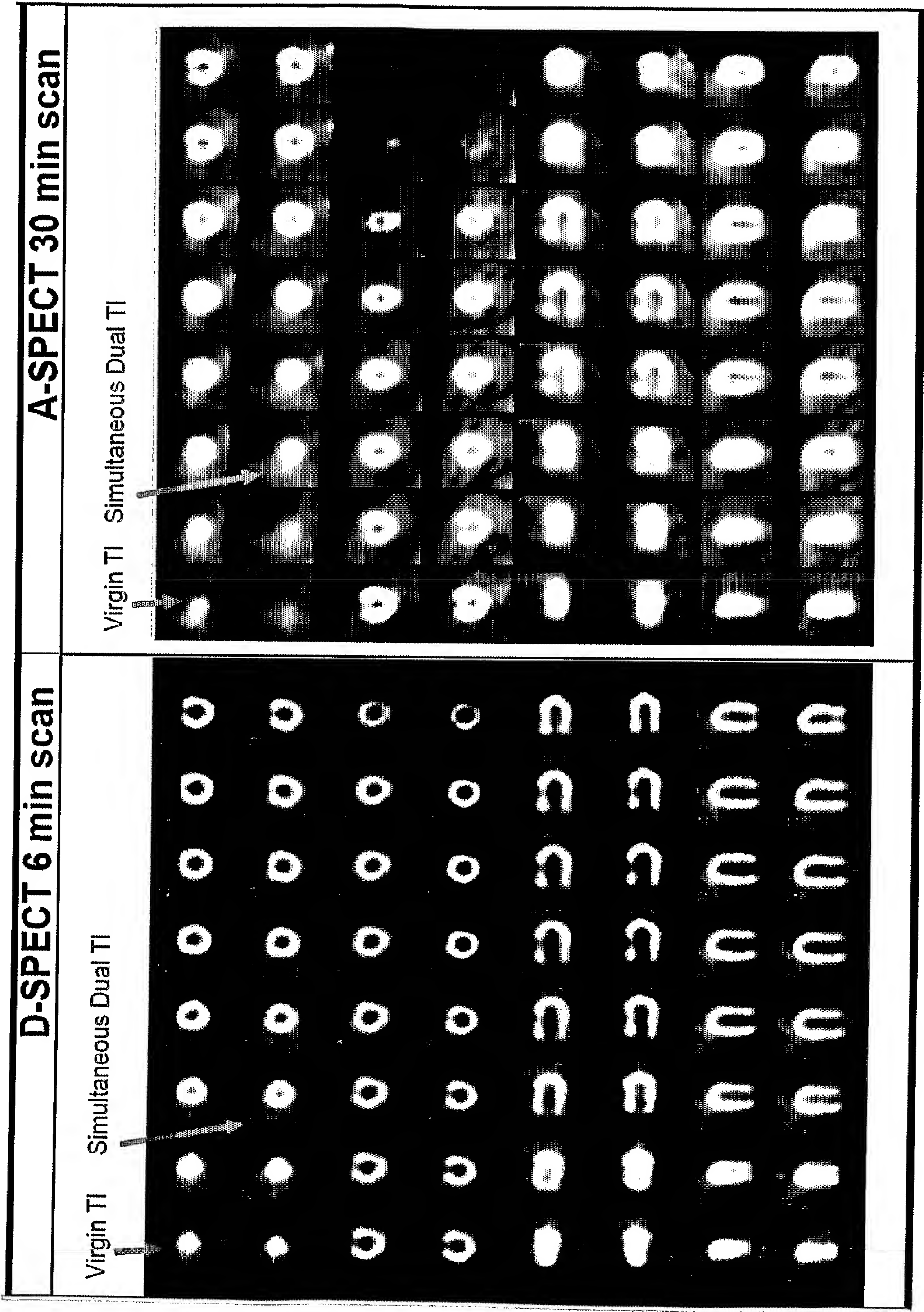


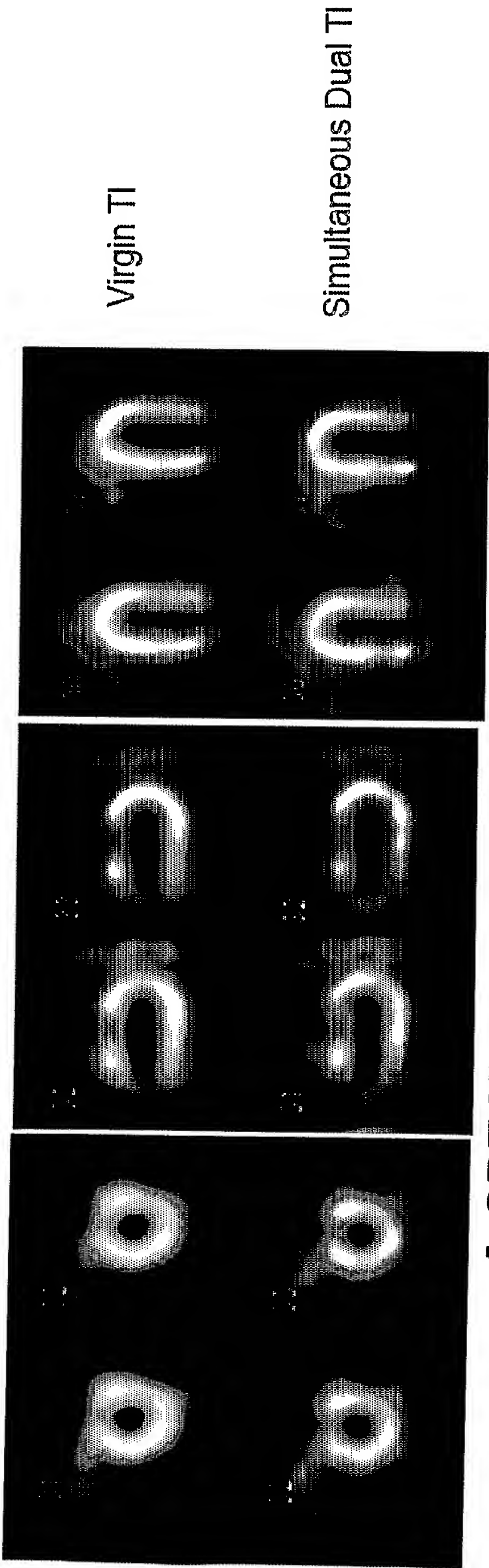
Fig. 108A

Fig. 108B



Fig. 109A

D-SPECT 6 min scan



A-SPECT 30 min scan

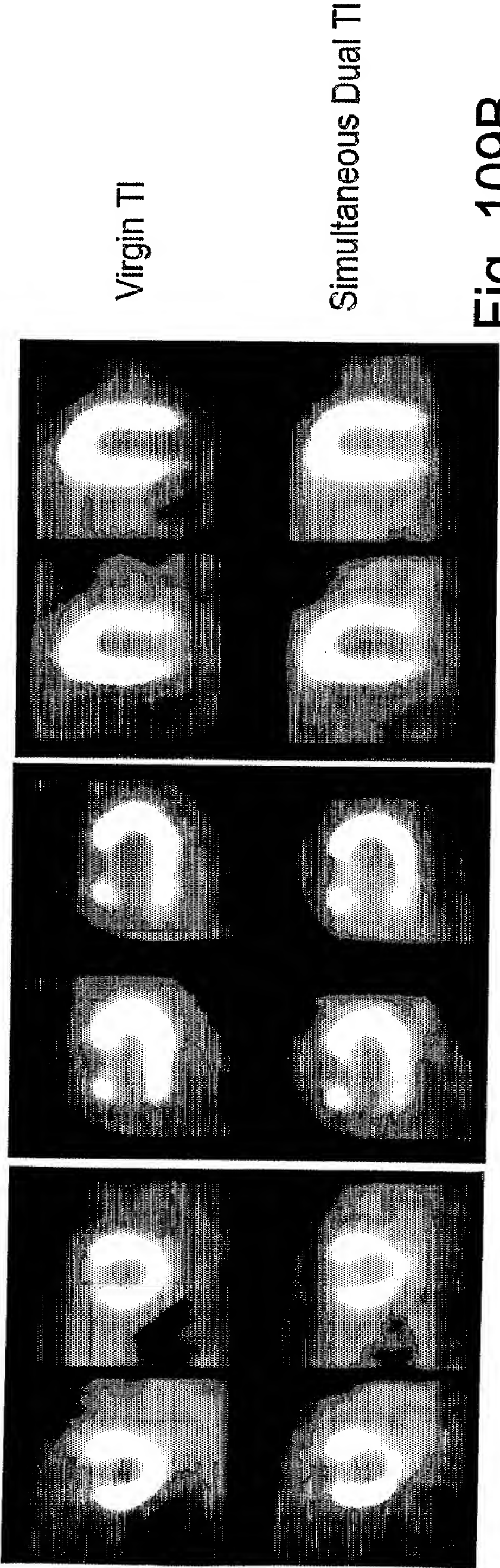
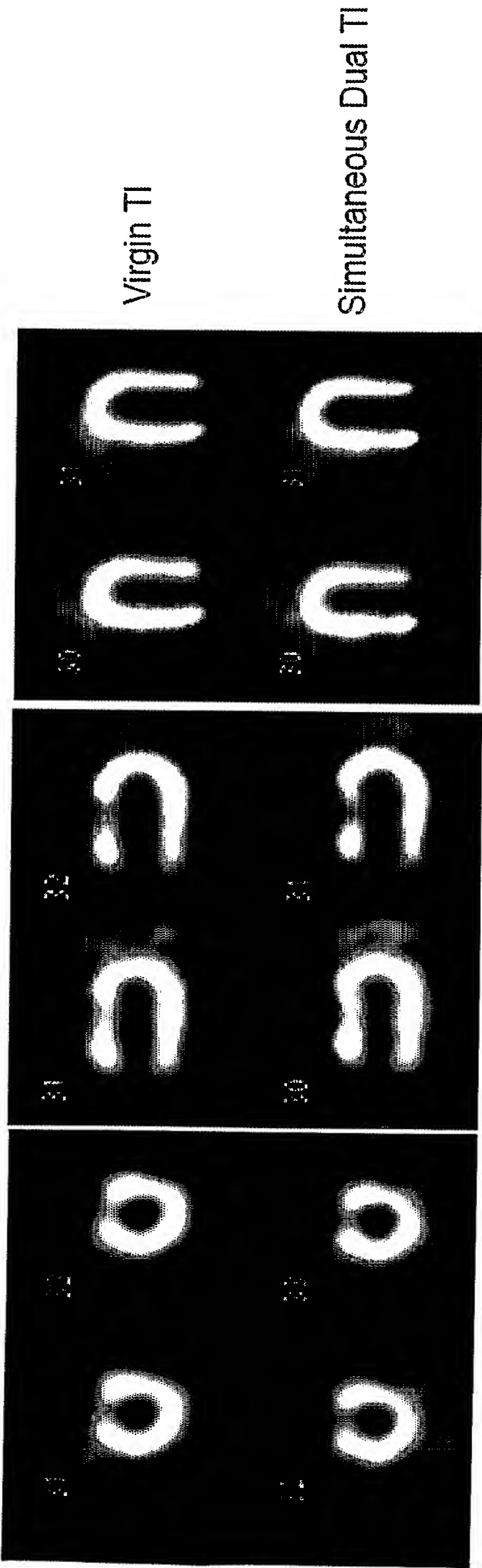


Fig. 109B

Fig. 110A

D-SPECT 6 min scan



A-SPECT 30 min scan

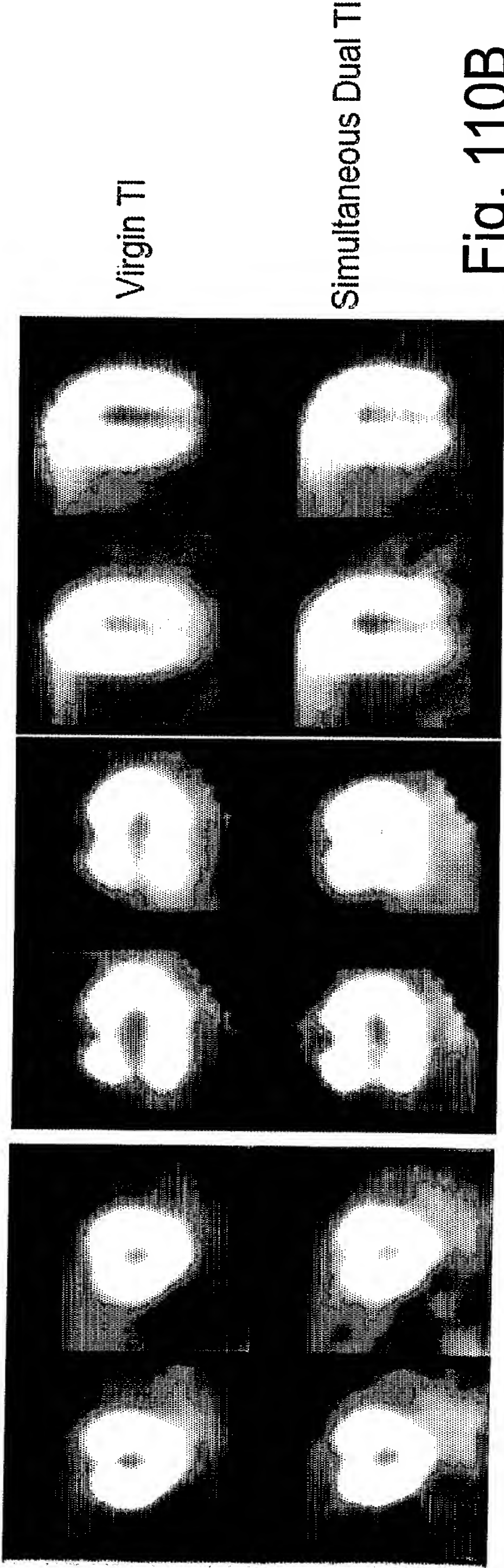


Fig. 110B